THE PERIPHERAL CIRCULATION IN HEALTH AND DISEASE

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PERIPHERAL CIRCULATION IN HEALTH AND DISEASE

A STUDY IN CLINICAL SCIENCE

BY

ROBERT L. RICHARDS, M.D.

Rockefeller Fellow in Medicine
Formerly Assistant Physician, Neurovascular Unit,
Gogarburn Hospital, Edinburgh

FOREWORD BY

J. R. LEARMONTH

C.B.E., Ch.M., F.R.C.S.E.

Professor of Surgery and Clinical Surgery University of Edinburgh

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PREFACE

THE greater part of the work of which this monograph is a record was done in the Neurovascular Unit at Gogarburn Hospital, Edinburgh, under the direction of Professor J R Learmonth I am indebted to Dr Andrew Davidson, Chief Medical Officer to the Department of Health for Scotland, and to Dr R Bailey, Medical Superintendent of the hospital, for permission to utilise the case records of patients admitted to the unit The illustrations have been prepared by the technical staff of the Wilkie Surgical Research Laboratory, University of Edinburgh the diagrams were redrawn from my originals by Mr C Shepley, and the photographs were taken by Mr A Paterson An immense amount of care and trouble has been expended in their preparation, and I wish to express my thanks to the artist, to the photographer and to Mr F W Pettigrew, all of whom gave me valuable assistance I have to thank Miss J B Gardner for typing the manuscript, for help in the arduous task of proof reading, and for much valuable advice on matters of grammar and syntax Dr A E Ritchie kindly read the proofs and gave me some helpful advice I am grateful to Mr Macmillan and Mr Parker of Messrs E & S Livingstone for their kindness and courtesy to a young and inexperienced author I would express my thanks to those patients who willingly submitted to multiple examinations For part of the time during which the work was in progress I was in receipt of a personal grant from the Medical Research Council

R L R

EDINBURGH
May, 1946

FOREWORD

DR RICHARDS' monograph presents a mass of information not readily accessible in any other form, and will, I feel sure, be welcomed by fellow-workers in this field, somewhat restricted though it may be. As he points out, the investigation began in an endeavour to collect physiological information in cases of war injury, but, as so often happens in research, gaps were found in fundamental knowledge, and after these had been made good to the best of his resources, we found that in our clinical work we were on surer ground in making diagnoses, planning treatment and estimating results

Clinical research of this productive kind is possible only when suitable cases are segregated The establishment of centres such as that in which Dr Richards and I worked together was due to the initiative of the Medical Research Council; the patients came partly through service channels and partly through the kindness of colleagues Every assistance was given by the medical superintendent of the hospital, Dr R Bailey, and by the Chief Medical Officer to the Department of Health for Scotland, Dr A Davidson In so agreeable and co-operative an atmosphere it was a pleasure to extend to Dr Richards certain facilities in my University Department, and to see reflected in our surgical work the benefit of clinical research carried out with so much care and devotion

J. R. LEARMONTH.

Department of Surgery,
University of Edinburgh 1946

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INTRODUCTION

"AND this indeed is the principal use and end of the circulation. It is that for which the blood is sent on its circuit, to wit, that all parts dependent on the primary innate heat may be retained alive, in their state of vital and vegetative being and apt to perform their functions" No better description of the vital function of the peripheral circulation could be found than in these words of William Harvey (1649) In his Harveian oration, the late Sir Thomas Lewis (1933) said "Harvey has been termed the Father of Physiology, he was much more than that, for his child was Clinical Science, out of which physiology and pathology were afterwards born"

Clinical science embodies the study of disease in all its aspects, but is concerned chiefly with studies upon disease as it exists in living man. "its central and unique province, most fundamental of all work pertaining to the practice of medicine, is that which concerns living men" (Lewis, 1934) As an example of the principles and practice of clinical science the writings of Sir Thomas Lewis are unique. In his studies upon the heart-beat, the peripheral circulation and the mechanisms of pain is to be found that "rigid adherence to truth which takes no heed of consequence but seeks knowledge for its own sake" The present study owes much to the stimulus of Lewis's writings

War brings into the foreground many medical problems which have remained in the background during years of peace, amongst such problems are those relating to injuries of the main nerves and blood vessels of the limbs The present study was begun towards the end of the first year of the second world war By a study of the peripheral circulation in normal limbs it was hoped that information would be obtained which might later be of value in determining the viability of limbs after injuries of the main blood vessels From this starting point the work progressed in many directions

A search of the literature revealed that there was still insufficient knowledge of the normal fluctuations of skin temperature in the limbs of man under varying environmental conditions, an opinion which was endorsed by Sheehan (1941) in a review of the physiology of the autonomic nervous system An attempt was made to remedy this defect, but before the investigations were complete, two more urgent problems obtruded themselves upon the field of study peripheral vascular disease and injuries of the peripheral nerves

Peripheral vascular disease is a generic term and includes a wide variety of conditions in which there is a pathological disturbance of the circulation in a limb Such diseases are not primarily maladies of war, but there is a strong belief that the circumstances of total war increase the normal strain upon the cardiovascular system and thereby raise the incidence of peripheral vascular disease Loss of resilience in the vascular tree is an inevitable accompaniment of old age In some cases this process is complicated by a degenerative change in the arterial wall (arteriosclerosis) which leads to a reduction in the calibre of the vessels by thrombosis Thrombo-angiitis obliterans is also the cause of degenerative changes in the blood vessels, the effects of which are similar to but more acute than those of arteriosclerosis; it is a disease of young and otherwise healthy adults whose services in war are urgently required by the armed forces and in industry Few would deny that this latter form

of peripheral vascular disease is one of the most distressing of maladies, little is known of its aetiology and in so many cases so little can be done to save the affected limb or alleviate suffering Here then is an example of that human need which as Lewis (1934) points out is always the first step in the acquirement of " knowledge that is to become useful to the health of mankind " The importance of syphilis as a cause of organic arterial disease must not be neglected A second large group of peripheral vascular disorders comprises those in which the circulation is impaired as a result of spasm of the vessel wall and, at least in the early stages, organic changes are absent Vasospastic disorders are, like thrombo-angiitis obliterans, affections of youth and may be the cause of serious disability in soldiers, sailors, airmen and others whose efficiency is vital to a nation's war effort

Injury offers unique opportunities for studies in hominal physiology The evolution of knowledge concerning the peripheral nerves is an excellent example of this Since the first centre for the treatment of nerve injuries was established by the Surgeon General of the Federal Armies in the American Civil War, the progress of knowledge may be represented by a somewhat uneven staircase in which each upward step corresponds to a time of human conflict The work of Weir Mitchell, Head and his colleagues, Trotter and Davies, Stiles and Stopford was all directly or indirectly stimulated by observations upon wounded men Since the last war there have been many advances in physiology Among these the development of electro-physiology, the increased knowledge of the autonomic nervous system and the studies of Lewis and others upon the peripheral circulation all have a direct bearing upon the problems of nerve injury At many centres both in this country and in America this new knowledge is now being applied to the solution of clinical problems and the writer has been privileged to take part in this work

A hazard of war is that man may be subjected to abnormal environmental conditions which would at other times be avoided or faced only after adequate protective precautions had been assured Such conditions may be provocative of disease An example is the syndrome which is observed in the hands or feet of those who are exposed to cold for prolonged periods Known in the last war as " trench foot," in this war it came to be known also as " immersion foot " on account of its prevalence in shipwrecked mariners who spent many days adrift in lifeboats or on rafts with their feet in cold sea water The author saw some of the earliest cases of this nature which reached this country after the sinking of an aircraft carrier during the Norwegian campaign in 1940 Subsequently several similar cases came under observation The syndrome is associated with a profound disturbance of the peripheral circulation and thus comes within the scope of the present study

This monograph therefore embodies studies upon the peripheral circulation in normal limbs, in the limbs of those suffering from peripheral vascular disease, in the limbs after injuries of the peripheral nerves and in the limbs of those who have been exposed to the effects of cold The original observations are preceded by a critical review of the literature upon the anatomy and physiology of the peripheral vasomotor system, and a description of the methods of study Each section is intended to be complete in itself, and, so far as is possible, references from one section to another have been avoided This has entailed some repetition, but, it is hoped, may have made the book more readable

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CHAPTER ONE

THE ANATOMY AND PHYSIOLOGY OF THE PERIPHERAL VASOMOTOR SYSTEM

INTRODUCTION

THE circulation in the limbs of man is so regulated that at all times it is adequate for local tissue needs and consistent with the requirements of the body as a whole. These two governing influences are frequently opposed, and to maintain a correct balance a complex vasomotor mechanism is required. This mechanism consists of the blood vessels themselves and those factors, nervous and humoral, which regulate blood vessel activity. The present study is concerned chiefly with the nervous regulation of blood vessel activity, and therefore in this review emphasis will be placed upon the role of the vasomotor nerves.

THE BLOOD VESSELS

The blood vessels of the human limb conform to a relatively constant anatomical pattern. Descriptions of this pattern and of abnormalities that may be considered physiological in that they do not influence the development, nutrition or vascular responses of the limb, may be found in any standard anatomical text-book. Excellent descriptions of the cutaneous vessels which are those most concerned with peripheral vasomotor activity are to be found in the monographs of Lewis (1927) and Krogh (1929). Lewis classifies cutaneous vessels as (strong) arterioles, minute vessels and deep veins. In addition to these vessels, mention must be made of arteriovenous anastomoses[1]. The presence of these structures in human skin was first observed by Sucquet in 1862, and subsequently Hoyer and Grosser demonstrated that they were particularly numerous in digits. Their relation to human physiology and pathology has been elaborately studied by Grant and Bland (1931) in this country, Masson and Popoff (1934) in France, and Clark (1938) and his associates in America. Arteriovenous anastomoses consist of muscular walled and richly innervated channels forming direct communications between arterioles and venules. When they are open, blood flows rapidly through them and by-passes the minute vessels of the capillary bed. In the extremities their distribution is predominantly acral. Grant and Bland (1931) counted 501 per square centimetre on the nail bed of the index finger, whereas the count fell below 100 on the proximal phalanges and palm of the hand. In the more proximal portions of the limbs they were almost absent. It is generally believed that the function of arteriovenous anastomoses is to regulate both local and general temperature (Grant and Bland, 1931; Popoff, 1934);

[1] Correctly arteriolo-venous anastomoses.

when open they provide a greatly increased cutaneous circulation which raises local temperature and increases heat dissipation Clark (1938) has demonstrated that new arteriovenous anastomoses may develop in response to a local increase in blood flow, and that when the blood flow returns to normal they revert to capillary status If this is true, it would be interesting to have comparative figures for the number of anastomoses in those who are habitually cold- and warm handed respectively

The histological structure of the blood vessels requires little description Arteries varying in size from the subclavian and femoral to the arterioles are endothelial lined tubes with walls of smooth muscle and elastic tissue The endothelial lining, or intima is a single layer of cells arranged longitudinally upon a layer of elastic tissue, the internal elastic lamina The middle coat, or media, is formed by a varying proportion of elastic tissue and muscle , the former predominates in the larger arteries and the latter in the smaller and more active vessels The outer coat, or adventitia consists of connective tissue which blends with that surrounding the blood vessel In the deeper layers of the adventitia are the vasa vasorum which nourish the artery Veins are also endothelial lined tubes but, in contrast to the arteries, their wall is chiefly composed of white fibrous tissue and contains less muscle and elastic tissue The veins of the limbs contain valves so placed that they direct the blood proximally The capillaries are thin walled endothelial channels surrounded by a very fine layer of delicate connective tissue, the *perithelium*

For many years it was doubted whether capillaries which have no muscular coat were capable of active contraction or responded passively to changes in the calibre of the arteries and arterioles The experimental researches of Krogh (1929) demonstrated the reality of active contraction of capillaries, but the mechanism responsible for this contraction is still a subject of controversy Krogh (1929) believed that the branching cells originally described by Rouget (1879) which are always found in close relation to the capillaries, were responsible for causing capillary contraction Beecher (1936), working in Krogh s laboratory, suggested that two mechanisms were responsible *constriction of the capillary wall by Rouget cells* and narrowing of the lumen by swelling of the nuclei of endothelial cells Many observers consider that the Rouget cells are not an integral part of the capillary wall but belong to the macrophage system (Clark, 1939) This hypothesis is supported by the observations of Clark and Clark (1925) and Sanders *et al* (1940), who found that Rouget cells did not participate in the contraction of amphibian (tadpole) or mammalian (rabbit) capillaries respectively Observations in man have not helped to solve this problem, but there is abundant evidence that human capillaries are also capable of independent contraction The observation of Leriche and Policard (1920) that *contraction of the capillaries of the nail bed followed stimulation of the peri* arterial sympathetic fibres on the brachial artery is open to the criticism that the capillary contraction might be a passive response to the contraction of arteries and arterioles The clinical researches of Lewis and his colleagues (Cotton, Slade and Lewis 1917 Lewis, 1927) and more recent observations by Bordley *et al* (1938), are pertinent to the present study as they prove that the cutaneous capillaries in man may contract

" It is a characteristic feature of the blood vessels of the human skin that there is no very sharp distinction between the smallest arterioles, the capillaries proper and the venules " (Krogh, 1929) For practical purposes it is therefore most convenient to adopt Lewis's classification and group all vessels smaller than the strong arterioles under the general heading " minute vessels "

THE VASOMOTOR NERVES

The nervous control of the blood vessels, like that of all hollow viscera with smooth muscle in their walls, is by the autonomic nervous system Although it is true that the calibre of certain vessels, notably those in skeletal muscle, is regulated chiefly by locally produced metabolites, the available evidence is strongly in support of the view that all blood vessels, arteries, veins and capillaries, are subject to some degree of nervous control

1. HISTORICAL

Credit for the discovery of the vasomotor nerves is usually given to the French physiologist Claude Bernard, who in the year 1852 demonstrated that section of the *cervical sympathetic in the rabbit caused an increase in the temperature of the ear* on that side (Olmsted, 1939) McDowall (1938) and others have pointed out that *the power of arteries to contract had been known to many observers since the early* years of the 19th century The French anatomist Xavier Bichat (1802) had noted *the intimate relation between the "systeme des ganglions" (as the sympathetic* nervous system was then known) and the blood vessels Henle (1840) observed that *sympathetic fibres, apparently motor in nature, were distributed particularly along* the blood vessels, and concluded that the middle coat of the arteries was muscular *and contracted in response to nervous stimuli*

When Bernard published his results on section of the cervical sympathetic, he *attributed the rise in temperature and the vasodilatation which he observed in the* rabbit's ear to alterations in metabolism within the tissues, and did not realise that by *interrupting the sympathetic fibres he had caused a vasomotor paralysis* The significance of his observation was grasped by Brown-Sequard, who in the same year (1852) showed that stimulation of the *peripheral cut end of the sympathetic caused* vasoconstriction and a fall in temperature of the skin of the ear Although Bernard later published similar observations, he maintained until the end of his life that the thermal and vascular changes which followed interference with the sympathetic were secondary phenomena, and that the primary change was an alteration in local metabolism (Olmsted, 1939) The belief that the changes were those of vasomotor paralysis was, however, upheld by Brown-Séquard in America, Budge (1853) in Germany, and Waller (1853) in England The influence of the nervous system on the blood vessels also attracted the attention of Laster (1858) during his early researches on inflammation, and he described with great accuracy and detail the changes in the arteries of the web of a frog's hind limb following destruction of portions of the spinal cord and section of anterior spinal roots

These experimental observations were followed by clinical descriptions c in which interference with the sympathetic trunk resulted in cutaneous vas disturbances Gairdner (1855) described the case of a man with an aneurysm thoracic aorta which was associated with unilateral flushing of the face Ogle described a case in which the sympathetic chain had been destroyed by a gumn recorded temperature observations upon the two sides of the face He ol that although the ear on the affected side was habitually the warmer of th under two sets of circumstances—after exercise and when the patient was fev the normal ear was the hotter This led him to postulate the existence in the c sympathetic of vasodilator as well as vasoconstrictor fibres[1] Weir M Morehouse and Keen (1864) and Vulpian (1875) described cases in which the s thetic chain was injured by gunshot wounds, and the vasomotor disturbances followed these injuries are described with great clinical accuracy

Little further advance was made until the physiological researches of C (1916) and Langley (1921) provided a clear conception of the form and functi the autonomic nervous system and thus paved the way for operative proc designed to modify visceral function As will be explained later, the surgeor came to realise that results obtained in experimental animals could not be trans directly to man, and so within the last twenty years the hominal physiology vasomotor system has been oriented from a study of the results of surgical oper

2 CENTRAL CONTROL

Although man is unable to exert any voluntary influence over the peri blood vessels, the influence of emotion on the cutaneous blood vessels pronounced that the existence of some central coordination of vasomotor a cannot be doubted Thus there are the pallor of fear, pain and other unpl emotions, the vasodilatation of excitement and rage and the emotional fl associated with embarrassment In certain patients who exhibit the Ra phenomenon, an attack of spasm of the digital arterioles may be precipitat emotion under circumstances which are otherwise favourable for the onset o an attack The higher centres responsible for the control of vasomotor functi man have not as yet been defined with any degree of clarity, and considerable exists as to the relative importance of the roles played by the cerebral cortex a autonomic centres in the hypothalamus

The Cortex.—Evidence obtained by experiments on the higher apes plac cortical control of vasomotor activity in the pre-motor area Removal of thi results in a decreased surface temperature of the contra-lateral limbs and a distur of peripheral vasodilatation in response to a raised environmental tempe (Kennard, 1934 and 1935 , Pinkston and Rioch, 1938)

In man, observations which have been made on cases of hemiplegia and cerebral lesions present a somewhat confusing picture of the nature of cortical motor control Gowers (1888) observed that cases of hemiplegia, and trau lesions in the neighbourhood of the "central gyrus," were frequently accomp

[1] According to McDowall (1938) Schiff had previously made a similar suggestion as a re experimental work upon the rabbit s ear

by vasomotor disturbances in the contra-lateral extremities In the early stages of such a lesion the paralysed extremities showed a raised surface temperature, but this was not maintained and the late results were cold, cyanosed, spastic limbs Zenner and Kramer (1909) described a remarkable case in which, during two operations for the removal of a meningioma in the left central region, the right radial pulse was noted to become imperceptible while the left pulse remained of good volume On both occasions the right pulse had returned to normal by the next day Bury (1935) quoted a case where a lesion of the left internal capsule produced a remarkable degree of vasoconstriction in the right arm , the radial and brachial pulses became impalpable and the blood pressure in that arm could not be recorded This state of affairs was transitory and within a few days the vasomotor state of the two arms was similar Ellis and Weiss (1936), on the other hand, who made a very careful study of the vasomotor state of the limbs of hemiplegic patients, demonstrated that the circulation to such limbs was elevated, and might remain elevated for as long as 13 years after a cerebro-vascular accident Similarly Kennard et al (1934) described a case in which a tumour of the right pre-motor area was associated with " forced grasping," spasticity, clumsiness and a raised surface temperature in the left hand In this case the vasodilatation persisted after removal of the tumour Stimulation of the cerebral cortex in man has failed to reveal any valid evidence of a cortical vasomotor centre (Penfield and Boldrey, 1937)

Observations of resting skin temperature and the vasomotor responses of the digits to heating and cooling the indifferent limbs were recorded in a series of hemiplegic patients by Uprus et al (1935) These workers found that there was no constancy in the temperature differences of the two sides , the affected limbs might be higher in temperature one day and lower in temperature the next The reflex responses differed little from the normal , the only slight difference noted was in the rate of cooling and this could be accounted for by the abnormal attitudes of the spastic limbs More delicate observations were made by Sturup et al (1935). Using a plethysmographic technique, they showed that the vasoconstrictor responses which can be elicited in normal digits by extrinsic stimuli (cold, pain, noise), intrinsic stimuli (deep breathing, lowering of blood temperature) and mental effort were unaltered by lesions of the cerebral hemispheres no matter where these were situated or what was the degree of motor or sensory dysfunction This was true whether the stimuli were applied to an affected limb and the vasomotor responses recorded on the normal limb, or vice versa Williams and Scott (1939) found that following the removal of the whole of one cerebral hemisphere the vasomotor responses in the digits were equal on the two sides

The Hypothalamus—The results of recent research are unanimous in placing the centre responsible for the regulation of body temperature in the hypothalamus The experimental observations upon which this assumption is based have been reviewed by Beattie (1935), Ranson (1940) and Fulton (1943) It is probable that there are two heat regulating centres a centre which prevents overheating situated between the optic chiasma and the anterior commissure, and a centre situated more caudally which protects the body against excessive heat loss on exposure to cold

In man, peripheral vasodilatation and vasoconstriction are, with sweating, the chief factors concerned in the conservation or dissipation of heat from the body surface It is therefore to be expected that these hypothalamic centres will exercise considerable influence upon the cutaneous blood vessels of the extremities Clinically, lesions in the neighbourhood of the hypothalamus frequently result in disturbances of the regulation of body temperature Depending upon the site and nature of the lesion, hypothermia, hyperthermia or poikilothermia may result (Dott, 1938; Davison, 1940) In only two cases with known hypothalamic lesions have disturbances of the vasomotor state of the limbs been noted In Penfield's (1929) case of "diencephalic epilepsy" marked flushing of the extremities was noted during the attacks, and Peet and Kahn (1936) described a case where vasospastic attacks and cyanosis of the extremities accompanied a hypothalamic tumour

Marquis and Williams (1938) investigated the vasoconstrictor responses in the digits in response to noxious stimuli They found that in lesions of the central nervous system caudal to the hypothalamus the response was directly proportional to the patient's subjective appreciation of the stimulus (that is, pricking over a hyperaesthetic area produced a greater response and pricking over a hypaesthetic area a less response than that which followed the application of the same stimulus to a normal area) If the lesion was situated above the level of the hypothalamus, then the vasomotor response did not alter with the patient's subjective feelings From these observations and those of Sturup *et al* (1935), they conclude that in man the vasomotor reflex arc is complete at a level caudal to the sensory thalamus

Considered as a whole these observations suggest that the main centre for the regulation of the vasomotor state of the extremities lies in the hypothalamus It is difficult to say what controlling influence the cortex may exert over the fundamental hypothalamic centre, and whether this is of an active or inhibitory nature The conflicting results obtained by different observers probably depend upon the exact site of the lesions, and whether or not these have resulted in a complete destruction of the cortical cells concerned, or of their efferent neurons Whatever the nature of the cortical control, it is of secondary importance and does not play a significant part in the normal vascular responses which are concerned with the regulation of body temperature and the application of noxious stimuli

Pathways in the Brain Stem and Spinal Cord —The descending pathways from the hypothalamus which are concerned in the regulation of vasomotor activity have not been defined with any degree of accuracy Experimental work by Beattie *et al* (1930) in the cat placed the descending fibres from the hypothalamus in the ventral portion of the posterior longitudinal bundle (medial longitudinal fasciculus) with some fibres entering into and ending in the reticular formation of the medulla, while the others passed on to terminate in the lateral column of the spinal grey matter Some of the fibres crossed the mid line while others descended uncrossed It is stated (Kuntz 1934) that unilateral section of the spinal cord at the level of the upper cervical segment in cats results in a paralysis of the vessels of the extremities on the side of the lesion only Ascroft (1937), on the other hand, found that after section of the left cerebral peduncle in the monkey there was a sympathetic paralysis on the

right side of the body as measured by the development of adrenalin sensitivity in the vessels of the digits. List and Peet (1939) have made an extensive clinical study of the distribution of the sympathetic fibres subserving sweating in man. They consider that these fibres decussate in the upper portion of the pons and that below this level they descend in the reticulo-spinal tracts, particularly the lateral reticulo-spinal tract. Thus, lesions of the lower pons or medulla (for example, thrombosis of the posterior inferior cerebellar artery) resulted in an ipsilateral hemihypohidrosis, whereas a unilateral lesion of the upper pons might produce a bilateral symmetrical hypohidrosis of both trunk and extremities. They found that in most cases the hypohidrosis was accompanied by a partial degree of vasoconstrictor paralysis and a Horner's syndrome on the affected side, so that it is likely that the vasomotor and pupillo-dilator fibres pursue a similar course. Duthie and Mackay (1940) have also recorded ipsilateral vasoconstrictor paralysis following thrombosis of the posterior inferior cerebellar artery. Stead *et al* (1942) found that after thrombosis of the posterior inferior cerebellar artery only certain vasomotor functions were disturbed; vasoconstriction in response to body cooling was impaired, but vasodilatation and vasoconstriction in response to a deep breath and painful stimuli remained unaffected.

It would therefore appear that the cutaneous blood vessels of the extremities are directly under the control of the hypothalamic autonomic centres, and the medullary vasomotor centres described by Ranson and Billingsley (1916) are probably concerned only with the more vital activities of the heart and great vessels.

In the spinal cord the descending vasomotor fibres lie immediately anterior to the pyramidal tract, between it and the anterior horn of the grey matter, the fibres for the upper limb lying near the mid-line and those for the lower limb to the outer side (Ascroft 1937). These neurons form synapses with cells in the lateral horn of the grey matter, and from these the pre-ganglionic neurons arise. The lateral horn is most fully developed in that section of the cord which is associated with the thoraco-lumbar outflow and the white rami communicantes.

3. THE PERIPHERAL PATHWAY

(*a*) **Vasoconstrictor Nerves.**—Vasoconstrictor nerve fibres destined for the extremities leave the lateral horns of the grey matter of the spinal cord as pre-ganglionic neurons of the sympathetic system. They emerge via the anterior roots and white rami communicantes and enter the paravertebral ganglionated chains in which they may pass for varying distances either cranially or caudally before forming synapses with the postganglionic neurons. From the ganglia postganglionic neurons run via the grey rami communicantes to the spinal nerves and are distributed with these.

(i) *Upper Limb.*—The actual roots by which the preganglionic fibres which are concerned with vasomotor activity in the upper limb leave the spinal cord have recently been the subject of considerable discussion. The original hypothesis was based on the pioneer work of Langley on the sympathetic nervous system of the cat. According to his observations, the anterior roots concerned in the sympathetic innervation of the fore limb were those from T4 to T9 inclusive (Langley, 1921). In the dog,

Bayliss and Bradford (1894) found that the outflow extended from T3 to T11, but that the contribution from the highest and lowest of these roots was very small In man the problem is intimately linked with that of complete surgical denervation of the blood vessels of the upper limb, and since operations on the sympathetic nervous system have become a recognised therapeutic procedure, it has been realised that observations on the lower mammals cannot be transferred directly to man Recently Sheehan and Marazzi (1941) have stimulated the anterior spinal roots in the monkey and recorded action potentials in the peripheral nerves by means of a cathode ray oscillograph Using this method, they find that C waves characteristic of autonomic fibres can be obtained from the median, ulnar and radial nerves when the anterior roots from T4 to T8 inclusive are stimulated They consider that the major preganglionic outflow to the upper limb comes from T5, T6 and T7

These results are more likely to be applicable to man and would be in keeping with modern surgical teaching Gask and Ross (1937) place the outflow in the roots from T4 to T9 Foerster (1939) has stimulated the anterior roots in man and observed that stimulation of T1 or T2 produced vasoconstriction in the face but no vasomotor changes in the arm Stimulation of the roots from T3 to T6 and sometimes of T7 produced vasoconstriction in the arm When the anterior roots below this level were stimulated vasomotor changes were not observed in the arm Kuntz and his co-workers (Kuntz *et al*, 1938, Kuntz and Dillon 1942) believe that the first thoracic root supplies preganglionic fibres to the upper limb In the cat and rhesus monkey after removal of the second and third thoracic segments of the sympathetic trunk reflex vasoconstriction may still be demonstrated in the digits of the upper extremity It has even been suggested (Kirgis and Kuntz, 1942) that in some cases the eighth cervical root may carry preganglionic fibres destined for the brachial plexus Few surgeons would agree with these findings In the usual preganglionic sympathectomy of the upper extremity (White and Smithwick, 1942) the first thoracic root and stellate ganglion are left intact, and in a large number of cases observed after this operation the writer has been unable to demonstrate any reflex vasomotor activity in the denervated limbs

A contribution from the second thoracic root is more likely Any such contribution is not always of major importance since it has been shown in one case that when the highest intact anterior root is T3, the vasomotor responses in the hand are not significantly altered (Learmonth and Richards, 1943) Recent work on anterior root stimulation in man by Ray *et al* (1943) suggests that Foerster's findings with regard to T2 are not always applicable These workers studied a series of 16 cases in which the anterior roots were stimulated at operation and sympathetic activity in the upper limb measured by changes in skin resistance in the hand The upper limit of the preganglionic outflow was found to be T2 in 10 cases, T1 in 1 and T3 in 1, while the lower level varied between T7 and T10 There might be a difference in level of one segment in the outflow to the two sides in the same person Stimulation of any one root taking part in the outflow resulted in a change throughout the whole limb, that is there is no evidence of a segmental sympathetic innervation at this level These results explain why in some cases, after a preganglionic sympathectomy

performed by Smithwick's method, in which the second thoracic root is inadvertently left intact, the upper limb appears to be completely sympathectomised (personal observation), and yet in others sweating and vasomotor activity are almost normal (Atlas, 1941 , personal observation)

The situation of the synapses between the preganglionic and postganglionic neurons is also a little doubtful Langley's original analysis placed these in the inferior cervical and first thoracic ganglia, but it is probable that in man the synapses extend more caudally, at least as low as the second thoracic ganglion and even lower (Sheehan, 1941) Hyndman and Wolkin (1942) believe that all sympathetic fibres going to the upper extremity pass through the second thoracic ganglion, and that to secure complete denervation of the blood vessels of the limb it is necessary to remove this ganglion alone Goetz and Marr (1944) have recently recorded some observations in support of this hypothesis

Grey rami to the brachial plexus are very numerous Gask and Ross (1937) state that as many as 12-17 rami join the roots of the plexus and that the origin and distribution of these are inconstant Rami to the brachial plexus come chiefly from the middle and inferior cervical ganglia and from the first thoracic ganglion The presence and situation of the middle cervical ganglion are not constant Axford (1927) and Kirgis and Kuntz (1942) describe a " high " and a " low " type of middle cervical ganglion The inferior cervical and first thoracic ganglia are frequently fused to form the stellate (cervico thoracic) ganglion Detailed accounts of the grey rami to the plexus are given by Axford (1927) and Hovelacque (1927) , the description which follows is taken from the latter Rami from the middle cervical ganglion, or from the sympathetic chain at the level of the sixth cervical vertebra, pass to the fourth and fifth cervical nerves The stellate ganglion distributes rami to all the roots which help to form the plexus The fifth, sixth and seventh cervical nerves commonly receive one or occasionally two small rami, but the eighth cervical may receive three rami, one of which is frequently very large, and the first thoracic nerve may receive as many as five rami Woollard and Weddell (1934) found that the eighth cervical nerve received the most sympathetic fibres

Occasionally rami may reach the brachial plexus without traversing either the middle cervical or stellate ganglion Kuntz (1934) has described an intra-thoracic ramus from the second thoracic ganglion which joins the first thoracic nerve More recently Kirgis and Kuntz (1942) have described another ramus communicans which arises from the third thoracic ganglion and may either join the second thoracic nerve central to the site of the origin of its rami, or else pass to the second thoracic sympathetic ganglion, thus providing an additional pathway through which postganglionic fibres may reach the upper limb These anomalies are of considerable surgical importance

In addition to the branches to the mixed peripheral nerves, the sympathetic chain, and particularly the stellate ganglion, provides a series of branches which join the subclavian artery directly and are distributed in its adventitial coat These fibres cannot extend along the artery for any considerable length, as it is found that division of an artery is not associated with any appreciable diminution in the number

of nerve fibres in the adventitial coat distal to the site of division (Kramer and Todd, 1914 , Kerper, 1927) It is unlikely, therefore, that such fibres play any part in the normal vasomotor reactions at the periphery of the limb Nerve fibres reaching the artery in this way will remain intact after interruption of the peripheral nerves, and may form a relay in the pathway through which a damaged artery can impose spasm on collaterals when all the main peripheral nerves to a limb have been interrupted (Learmonth, 1943)

The distribution of branches from the peripheral nerves to the blood vessels of the extremities has been studied by Kramer and Todd (1914), Woollard (1926), Coates (1932), and Woollard and Weddell (1934) As they pass distally, the main nerve trunks of the limb distribute branches to the arteries, the branches becoming very much more numerous as the periphery of the limb is reached, and more numerous in relation to superficial as compared to deep vessels In the upper extremity most of the arterial branches come from the median, ulnar and radial nerves and their branches At the extreme periphery these nerves distribute vasomotor branches to the cutaneous vessels over the areas normally assigned to them as their territories of sensory distribution (Gilding, 1932 , Woollard and Phillips, 1932) It is probable that, as in the case of afferent fibres, there is a considerable overlap of vasomotor nerves from one nerve territory to that of the adjacent nerves (Richards, 1943)

Sympathetic vasoconstrictor fibres in the limbs are distributed chiefly to cutaneous blood vessels, but animal experiment indicates that vessels in the muscles also receive vasoconstrictor fibres from the nerves which supply the muscles with their motor fibres (Gilding, 1932) In man, Barcroft *et al* (1943) have recently demonstrated that the median, ulnar and radial nerves carry some vasoconstrictor fibres to the vessels of the forearm muscles

The nerve fibres which reach the blood vessels via the peripheral nerves consist of both afferent sensory (medullated) and efferent sympathetic vasoconstrictor (non-medullated) fibres In the arteries there is a rich adventitial plexus consisting of both types of fibres In the large proximal vessels non medullated fibres predominate (presumably as a result of the direct contributions from the sympathetic chain), but distally medullated fibres are relatively more numerous until the arterioles and minute vessels are reached when fine non medullated fibres again predominate Medullated fibres are to be found only in the adventitia where they have free nerve endings morphologically similar to sensory nerve endings elsewhere in the body Non medullated fibres originating in the adventitial plexus extend into the media where they form a true nerve net surrounding the smooth muscle cells This network is continuous throughout the length of the artery, and there is no evidence of a segmental innervation Fine neuro fibrils arising from the nerve net make contact with the muscle cells always at a point directly opposite the nucleus , intra-cellular nerve endings are not seen The arterioles are invested by a rich sympathetic innervation, and from this, fine non medullated fibres extend into the capillary bed where they end in close relation to, but not in, the endothelial walls of the vessels The innervation of the veins is similar to that of the arteries In man, ganglion cells are not observed in the blood vessels of the extremities (Woollard, 1926 , Busch, 1929)

An excellent review of the innervation of the blood vessels of the limbs has been published by Stopford (1931)

(ii) *Lower Limb*—The general pattern of the vasomotor innervation of the lower limb is similar to that described above The original observations on the cat and the dog placed the preganglionic outflow in the anterior roots from the eleventh thoracic to the second or third lumbar (Bayliss and Bradford, 1894 , Langley, 1921) Sheehan and Marazzi (1941) find that in the monkey the outflow is more restricted, being confined to the roots from T12 to L3 with the major contribution from the first three lumbar segments It is probable that in man the outflow, like that in the monkey, is of the more restricted variety, but most surgeons place the upper limit of the outflow at a higher level than T12—for example, T10 to L3 (Gask and Ross, 1937), T10 to L2 (Learmonth, 1939) Whatever the upper limit of the outflow, it is certain that the lower limit must be the third lumbar segment since there are no white rami caudal to that level The synapses between the preganglionic and postganglionic fibres for the leg lie in the ganglia from the third lumbar to the third sacral inclusive The third lumbar ganglion is important as it contributes a grey ramus to the fourth lumbar nerve which distributes sympathetic fibres to the inner side of the foot via the femoral and long saphenous nerves (Atlas 1940) Woollard and Weddell (1934) have shown that the grey ramus to the first sacral root is very much larger than any of the other rami to the lumbar plexus Thus the standard sympathectomy for the lower extremity in which the second, third and occasionally the first lumbar ganglia are removed (White and Smithwick, 1942), is predominantly preganglionic

Grey rami from the third lumbar ganglion caudally carry postganglionic fibres to the lumbar plexus, and the sympathetic fibres are distributed throughout the limb with the branches of the plexus In addition, the femoral artery, like the subclavian, receives a certain number of fibres which reach it via a peri arterial plexus continuous with that on the abdominal aorta and iliac vessels Studies on a limb shortly after the performance of a peri femoral sympathectomy demonstrate that these fibres do not extend peripherally for any distance (Blair *et al* , 1930) Accurate descriptions of the branches from the nerves to the arteries are to be found in the writings of Potts (1914) and Coates (1932) The sciatic nerve carries most of the vasoconstrictor fibres for the leg and foot, and these are distributed with its branches The femoral artery and its branches in the thigh receive their nerve supply from the femoral and saphenous nerves Although the standard anatomical text-books (Gray, 1942 , Cunningham, 1943) describe a branch from the obturator nerve to the femoral artery, other observers (Potts, 1914 , Blair *et al* , 1930 , Coates, 1932) state that this nerve supplies the obturator vessels only

(iii) *The Vasoconstrictor Mechanism*—Stimulation of the sympathetic outflow to the limbs causes widespread cutaneous vasoconstriction The strongest contraction takes place in the smaller arteries and arterioles, but other vessels also participate Experimental evidence that capillary contraction is controlled by the sympathetic and may be induced reflexly is to be found in the studies of Harris and Marvin (1927), Beecher (1936) and Sanders *et al* (1940) Constriction of veins in response to sympathetic stimulation has also been recorded (McDowall, 1938) Sympathetic

postganglionic fibres (those to the sweat glands excepted) belong to the group of nerve fibres which Dale (1933 and 1934) named adrenergic When such fibres are stimulated, the peripheral effects are similar to those produced by the release of adrenalin, in the present case, vasoconstriction It is now known that the substance which is released at sympathetic postganglionic nerve endings is not adrenalin but a closely related substance named sympathin According to Cannon, there are two sympathins, " sympathin E " and " sympathin I," the former producing an excitor and the latter an inhibitor effect (Cannon and Rosenblueth, 1937) Adrian and Bronk have shown that peripheral sympathetic nerve fibres carry persistent electrical discharges and that these are concerned chiefly with vasoconstriction (Adrian *et al*, 1932, Bronk, 1934) These impulses will cause a continuous release of the chemical transmitter at the nerve endings so that a certain degree of vasoconstriction will always be present in blood vessels innervated by the sympathetic This is the physiological basis of " vasoconstrictor tone " and will later be considered in more detail (*p 38*) *It is generally accepted that the impulses originate in cerebral vasomotor* centres, but it has been suggested, notably by Leriche (1939), that certain of the paravertebral sympathetic ganglia, particularly the stellate, are capable of autonomous activity or of acting as reflex centres There is, however, no definite proof that sympathetic ganglionic responses are part of the normal vasomotor mechanism in man (Bolton *et al*, 1937)

(*b*) **Vasodilator Nerves** —The evidence, both anatomical and physiological, for the presence in man of vasoconstrictor fibres is abundant With vasodilator fibres it is otherwise their presence has never been proved anatomically, and the physiological evidence which suggests their existence is almost entirely of an indirect nature A consideration of the possible existence of parasympathetic vasodilator fibres to such special organs as the salivary glands and the penis does not come within the scope of this review The only direct observation which suggests the presence of vasodilator fibres in the limbs is that of Sewall and Sanford (1890) These workers found that, on percutaneous stimulation of the ulnar nerve at the elbow, a weak stimulation produced vasodilatation in the little finger, whereas a stronger stimulus produced vasoconstriction As far as the writer is aware, this observation lacks confirmation It has been suggested that vasodilator fibres may reach the limbs by two routes —

(1) *Vasodilator Fibres in the Posterior Root System* —In 1876 Stricker demonstrated that stimulation of the distal cut ends of posterior spinal roots in the lumbar *region produced vasodilatation in the hind limb of the dog* Since that date the problem of efferent fibres in the posterior roots subserving vasodilatation has been a constant source of discussion Bayliss (1901 and 1923) who repeated and confirmed Stricker's experiments, showed that the nerve fibres concerned in this " antidromic " vasodilatation, as he called it, had no connexion with the sympathetic nervous system The fibres did not degenerate after section of the posterior roots, but did degenerate if the posterior root ganglia were removed, and he therefore concluded that their cells of origin were in these ganglia The problem was also studied by Langley (1923) who showed that antidromic vasodilatation was a peripheral

phenomenon in which only cutaneous vessels were involved In the cat's paw, if a plantar or digital nerve were stimulated, flushing was observed only in the cutaneous territory of that nerve, and there was a compensatory pallor of the rest of the foot Conversely if a plantar or digital nerve were cut and the appropriate posterior root then stimulated, flushing would take place in the paw except in the territory of the divided nerve He concluded by stating that the facts known at that time were insufficient to decide whether antidromic vasodilatation was produced directly by " afferent " fibres ending in and acting as effectors on the capillaries or indirectly by the release of metabolites at the endings of " afferent " nerve fibres The evidence, he believed, was in favour of the latter hypothesis

After section of the posterior roots the times for degeneration and regeneration of nerve fibres overlap to such an extent that anatomically it is very difficult to prove the existence of emergent posterior root fibres This aspect of the problem has been carefully studied by Westbrook and Tower (1940) who conclude " the concept that nerve fibres emerge from the spinal cord into the posterior roots in adult mammals including man is without foundation in anatomical fact or physiological necessity and may therefore be dispensed with " Be that as it may, physiologists support the hypothesis that a certain number of posterior root fibres are at any rate capable of transporting efferent impulses Barron and Matthews (1935) state that *as high a proportion as 40 per cent of posterior root fibres can carry centrifugally* directed impulses and Toennies (1938-39) has demonstrated that an " antidromic " discharge in such fibres may be induced reflexly by sensory stimuli applied to the ipsi lateral or contra lateral limb

The question therefore arises whether such fibres are those belonging to the normal afferent sensory system or to a separate and hitherto unrecognised group of fibres in the posterior root system Bayliss (1923) stated that the fibres concerned with antidromic vasodilatation were indistinguishable from fibres subserving Head's (1920) protopathic sensibility This problem has been investigated by more modern methods by Hinsey and Gasser (1930) and Bishop *et al* (1933) These workers recorded action potentials in the fibres concerned, and found them to be slow-conducting non myelinated fibres destined chiefly for muscle and not concerned with any of the afferent functions

This antidromic vasodilatation is a different type of vasomotor response from that produced by stimulation of the sympathetic vasoconstrictor fibres or the parasympathetic vasodilator fibres to the penis In the latter type of response stimulation produces a vasoconstriction or vasodilatation which rapidly reaches its maximum, is maintained so long as stimulation is continued, and fades rapidly when it ceases Antidromic vasodilatation is a prolonged and delayed response to a brief stimulus Furthermore if the circulation to a limb is arrested during the period of stimulation, the vasodilatation is prolonged and always exceeds the reactive hyperaemia which follows the circulatory arrest (Lewis and Marvin, 1927) This suggests that antidromic vasodilatation is the result of the release at nerve endings in the skin of a relatively stable chemical substance which is removed by the blood

stream Dale and Gaddum (1930) suggested that the substance concerned might be acetylcholine, and later Wybauw (1936) demonstrated that this substance was present in perfusion fluid returning from a limb in which antidromic vasodilatation was being induced Acetylcholine is, however, an exceedingly labile chemical substance as far as the body is concerned, and recent evidence (Lewis, 1942b) suggests that acetylcholine is released at the nerve endings and acts upon cells in the skin which in turn release more stable chemicals (H-substance), this second release is responsible for the vascular reaction

It is dangerous to transfer experimental findings of this nature directly to man, but in this instance there is *good clinical evidence for so doing* In herpes zoster, which is usually an affection of the posterior root ganglion, vasodilatation is observed in the cutaneous territory of the affected posterior root Cutaneous vasodilatation on stimulation of the posterior roots in man has been observed by Foerster (1933) The clinical researches of Sir Thomas Lewis have provided good evidence that nerve fibres belonging to the posterior root system are responsible for local cutaneous vasodilatation Local trauma to the skin mechanical, chemical or thermal, results in the production of the "triple response"—local vasodilatation, a spreading flare and the development of a wheal A similar response follows the intradermal injection of dilute solutions of histamine Lewis has shown that the flare is the result of an arteriolar dilatation and is dependent upon the integrity of the cutaneous sensory nerves Immediately after the division of a peripheral nerve (or the removal of the posterior root ganglion) a normal triple response can be obtained in the denervated area but if sufficient time is allowed to elapse for the nerve fibres to degenerate, a flare will not be observed A normal response is obtained in a sympathectomised limb Since the skin receives nerve fibres from the sympathetic and posterior root systems only, it is reasonable to suppose that the fibres of the latter provide the pathway through which this local vasodilatation is effected Lewis postulates that the arteriolar dilatation is the result of an "axon reflex" and that the pathways are those shown in the accompanying diagram (Fig 1)[1]

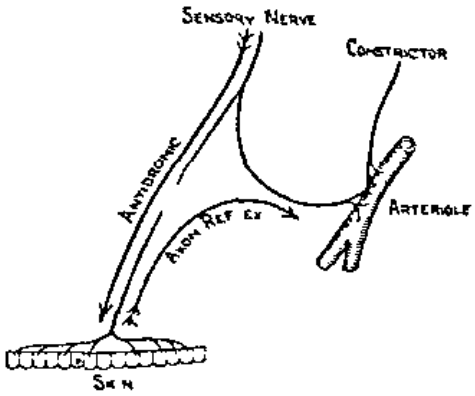

Fig 1
Diagram of Axon Reflex
Redrawn from Lewis (1927)

Lewis believes that there exists in the skin a plexiform arrangement of nerve fibres which belong to the posterior root system but are independent of those fibres carrying afferent impulses To this system he has given the name "nocifensor nervous system" and to it he attributes the vascular responses which follow local trauma and stimulation of posterior roots, and also the spreading hyperalgesia which can be observed following injury to the skin or the faradic stimulation of cutaneous nerves The nocifensor nerves are believed to be cholingergic, that is when stimulated they release acetylcholine at their endings This in turn

[1] This type of vasodilatation is hereafter referred to as "axonal vasodilatation"

acts upon the cells of the skin causing the release of other chemical substances which produce the local tenderness and vascular responses (Lewis, 1927, 1937, 1942a, b)

While it must be admitted that Lewis has produced convincing physiological evidence in support of his hypothesis, on anatomical grounds there are strong objections to the existence of the nocifensor nervous system A plexiform arrangement of nerve fibres in the skin such as Lewis postulates is known to exist, but the fibres taking part are believed to be those subserving cutaneous pain (Woollard *et al*, 1939) Further, as Walshe (1942) has pointed out, there is no evidence within the central nervous system of the existence of neurons belonging to this nocifensor nervous system, nor indeed is there any need for such neurons since the functions of the system are purely peripheral Lewis in fact postulates a system whose fibres are both receptor and effector, and whose activity is confined to a reflex arc which is complete at a level distal to the posterior root ganglion From what is known of the integrated functioning of the nervous system, such a mechanism appears to be unlikely There are nevertheless certain physiological and pathological phenomena associated with the cutaneous vasomotor system of man which are as yet inadequately explained, and it is well to preserve an open mind upon the problem of vasodilator fibres within the posterior root system

(ii) *Sympathetic Vasodilator Fibres*—The second route by which it has been suggested that vasodilator fibres may reach the periphery is along sympathetic pathways similar to those described above for the vasoconstrictor fibres In approaching this problem, it is necessary to consider the vasomotor responses of the muscles and the skin separately

The demonstration of sympathetic vasodilator fibres to muscle is dependent chiefly upon Dale's (1906) observation that after the administration of ergotoxine the vasoconstrictor response to the injection of adrenalin is abolished and is replaced by a vasodilatation This " adrenalin reversal," as it has been called, has been used in many experimental animals to demonstrate the existence of sympathetic vasodilator fibres Burn (1938) has pointed out that this is not a good guide to the existence of such fibres, since the " adrenalin reversal " can be obtained in certain animals (for example, the monkey) in which the effect of sympathetic stimulation is *always* constrictor According to Burn, sympathetic vasodilator fibres to the muscles are present in such athletic mammals as the hare and the dog, probably present but difficult to demonstrate in the cat, and absent in the rabbit and monkey These species differences make it difficult to transfer any of the experimental findings to man The control of the blood-flow to the skeletal muscles in man is predominantly chemical, the stimulus for vasodilatation during muscular exercise being provided by relatively stable metabolites produced by the muscle itself during activity (Grant, 1938) Nevertheless, certain sensory stimuli and small doses of adrenalin administered intravenously are known to produce vasodilatation in the muscular segments of the limbs (forearm and calf) This cannot be accepted as evidence for the existence of adrenergic sympathetic vasodilator fibres since the response persists and may even be enhanced after sympathectomy (Grant and Pearson, 1938, Wilkins and Eichna, 1941)

The arguments for the existence of sympathetic vasodilator fibres to the cutaneous blood vessels are all based upon the fact that after sympathectomy peripheral vessels will no longer respond reflexly to body heating The immediate result on a limb of sympathectomy is to raise the surface temperature of the hand or foot to that of full vasodilatation (34-36°C) This high level is not maintained and within 14 days the temperature will be found to have fallen considerably (28-30°C) If the sympathectomy has been complete and there is no local vascular factor to be reckoned with, this later temperature will be maintained indefinitely Warming of the trunk with the limbs exposed will now cause a rise in temperature in the normally innervated hand or foot, but no further rise will take place in the sympathectomised extremities (Lewis and Pickering, 1931) Grant and Holling (1938) have shown, and recently Doupe *et al* (1943) have confirmed, that if body heating in this manner is pushed very strongly, vasodilatation will take place in the more proximal portions of the limbs (forearm and leg), and that this is an active vasodilatation and not the result of release of vasoconstriction This response also is abolished by sympathectomy If the limbs are heated as well as the trunk so that the direct effect of local heat on the blood vessels comes into play as well as the indirect effect of the rise in body temperature, it is found that the normal and sympathectomised limbs will reach the same temperature, but that flushing of the skin will be absent on the side of the sympathectomy (Hyndman and Wolkin, 1941) These observations taken together afford fairly convincing evidence that, besides releasing normal vasoconstrictor tone, sympathectomy destroys vasodilator fibres which are partly responsible for the peripheral vasodilatation that normally follows a rise in body temperature The absence of cutaneous flushing in a sympathectomised area has been regarded as evidence for the presence of sympathetic vasodilator fibres to the capillaries (Hyndman and Wolkin, 1941)

Further evidence for the existence of sympathetic vasodilator fibres to the vessels of the digits has been obtained from patients showing the Raynaud phenomenon In some cases of this condition, a local nerve block may fail to produce a vasodilatation in the digits which are rendered analgesic In such cases if the nerve block is followed by an attempt to produce reflex vasodilatation by body warming it is found that vasodilatation does not follow in the digits affected by the nerve block, but that the other digits of the same extremity respond in a normal manner (Lewis and Pickering 1931 , Fatherree and Allen, 1938) The nerve fibres responsible for reflex vasodilatation have therefore been inactivated by the nerve block These fibres cannot be vasoconstrictor in function as the interruption of such fibres would prevent the passage of centrifugally directed vasoconstrictor impulses, thus tending to favour rather than prevent vasodilatation Unfortunately it has not been found possible to produce this effect in a normal limb, as local nerve block even when carried out in a very low environmental temperature, always results in a vasodilatation in the affected digits (Fatherree and Allen, 1938)

In conclusion, it may be stated that although there is no single observation which affords conclusive proof of the existence of vasodilator fibres in the peripheral nervous system of man, yet the evidence which has been presented above, considered

as a whole, offers considerable support to the hypothesis that there are vasodilator fibres within the recognised anatomical pathways of the sympathetic nervous system The existence of true vasodilator fibres outwith that system is more doubtful The evidence for the presence of vasodilator fibres in the posterior root system seems to be compatible with the suggestion recently put forward by Doupe (1943) that, when afferent nerve fibres are active, potent vasodilator metabolites may be released at their endings

THE LOCAL CONTROL OF BLOOD VESSELS

In addition to the control exerted by central nervous pathways, blood vessels are subject to a degree of local control If the mechanism of the axon reflex (p 14) is excluded, the local control of blood vessels is mainly chemical in nature There is no physiological evidence to support the hypothesis proposed by Braeucker (1929) and Leriche (1939) that in the arteries of man there exists an intramural nervous apparatus capable of independent automatic activity Chemical vasodilators and vasoconstrictors may either be produced locally in the part or be carried there by the blood stream Adrenalin is a typical example of the latter group, while histamine (H-substance) and the metabolites responsible for the hyperaemia of muscular exercise represent the second group Local thermal influences also affect blood vessel activity , warmth is a powerful vasodilator and cold a powerful vasoconstrictor Arteries with their muscular walls respond directly to the influence of warmth or moderate cold by dilating or constricting The reaction of the minute cutaneous vessels to local temperature changes is more complicated Lewis (1927) has shown that the tone of these vessels is directly increased by heat and lessened by cold Thermal changes also affect the concentration of vasodilator metabolites within the tissue spaces, and in this way produce indirect effects which are the opposite of their direct effects Local heat causes an increase in metabolites and cutaneous vasodilatation , cold reduces their concentration and causes an initial vasoconstriction with pallor of the skin, but, as the local temperature falls, the direct paralytic influence predominates and local reddening of the skin is observed

From the foregoing it will be appreciated that those vessels which supply blood to relatively large areas of the body, the arteries and arterioles, are predominantly under central control, either nervous or humoral, whereas the vessels responsible for the needs of the tissue cells, the minute vessels of the skin and the muscle capillaries, are regulated chiefly by locally produced tissue metabolites

SUMMARY AND CONCLUSIONS

The control of the blood vessels of the limbs is both nervous and humoral Vasoconstriction is effected chiefly through sympathetic pathways and a conception of the sympathetic innervation of limb blood vessels based upon a series of four neurons, cortico-hypothalamic, hypothalamico spinal, preganglionic and postganglionic, is presented (Fig 2) Preganglionic fibres for the upper limb leave the spinal cord in the anterior roots from T2 to T10 , the upper level of the outflow may

include the first thoracic root and the lower level varies between T7 and T10 The fibres for the lower limb issue in the roots from T10 to L2 inclusive The majority

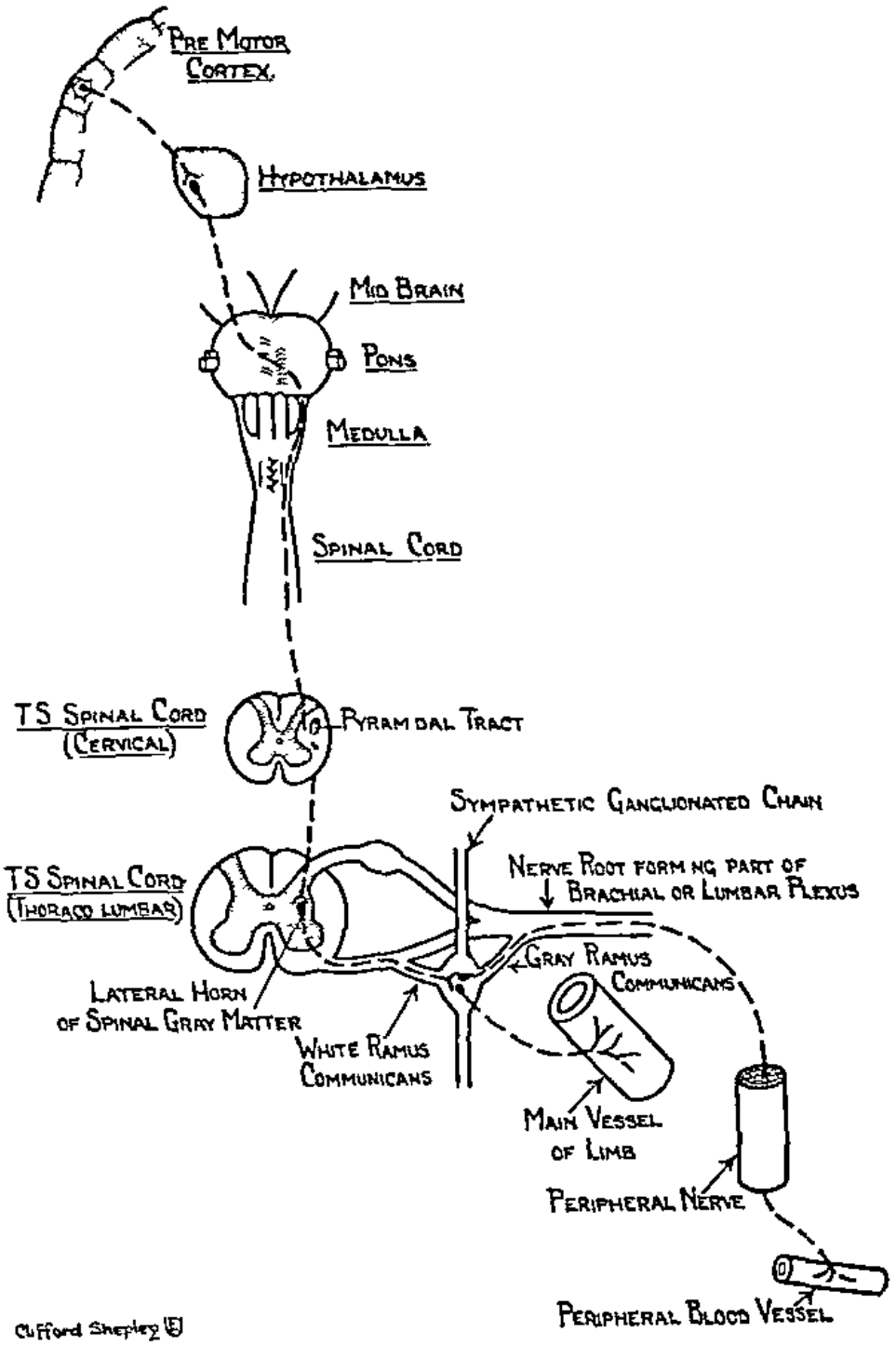

FIG 2
Diagram of Sympathetic Vasomotor Pathways to Limbs

of postganglionic fibres destined for the blood vessels join the peripheral spinal nerves and are distributed with these, but a minority reach the main artery of the limb

as direct branches from the paravertebral sympathetic ganglia Sympathetic vasoconstrictor fibres are predominantly distributed to the peripheral cutaneous vessels of the hand and foot Vasodilator mechanisms, on the other hand, are mainly humoral The increased blood flow to muscle in response to exercise, and cutaneous vasodilatation in response to local tissue needs, are both caused by the accumulation of relatively stable physiological metabolites The existence of vasodilator fibres in the peripheral nervous system of man is still not proven The evidence, in the author's opinion, is strongly in favour of the presence of such fibres within the sympathetic nervous system The possibility that vasodilator fibres exist outwith that system cannot be entirely disregarded

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CHAPTER TWO

METHODS OF STUDY

(With Particular Reference to the Recording of Skin Temperature)

IT is a common fallacy to assume that elaborate apparatus is necessary to determine the actual or potential degree of vasomotor activity in the limbs of man While it is true that mechanical aids such as the plethysmograph or thermocouple will elicit accurate and absolute data which clinical tests cannot provide, a relatively accurate estimate of the state of the circulation within a limb can be made by anyone who is observant and has the time and patience to carry out a few simple tests

At any given time the circulation to a limb is endeavouring to fulfil two main functions first, to provide for the metabolic needs of the tissues within the limb, and secondly, to maintain the temperature of the limb at a level which is, on the one hand, not injurious to the tissues, and, on the other, consistent with the needs of the body as a whole for heat conservation or dissipation Clinically, therefore, the state of the circulation may be determined either directly by observations on the blood vessels or indirectly by observing the nutrition and thermal state of the limb In the intact limb it is possible to observe directly the circulation in the main arteries (palpation of the pulse) and in the cutaneous vessels (skin colour and skin temperature) Only in the case of the circulation to the muscles is it necessary to rely upon indirect evidence, and it is therefore of prime significance that pain is an early symptom of muscle ischaemia By the cardinal clinical methods of inspection and palpation much may be learned concerning the vasomotor state of a limb

This study is concerned mainly with observations which have been obtained by mechanical means, but clinical observations have not been neglected Before proceeding to make any observations with the apparatus used, a careful clinical examination of the limb or limbs was always carried out The presence or absence of pulsation in the main arteries and collateral vessels was recorded The cutaneous circulation was studied by noting the colour of the skin with the limb horizontal, elevated, and dependent, and by determining the temperature of the limb by palpation It should be noted that skin temperature and skin colour must always be considered in conjunction a warm pale skin, a cyanosed warm skin and a red cold skin all have their own particular significance (Lewis, 1936) Skin colour depends mainly upon the state of dilatation of the cutaneous capillaries, skin temperature depends upon the rate of blood flow through the skin and is determined by the degree of dilatation of the arteries and arterioles With the limb horizontal and at heart level the rate of return of colour to an area which has been blanched by finger pressure is a simple and useful clinical test of the activity of the cutaneous circulation The degree of filling of the subcutaneous veins with the limb in a similar position is also a good

indication of the activity of the circulation The nutrition of the skin and its appendages frequently provides indirect evidence of the efficiency or otherwise of the cutaneous circulation, for example the atrophic shiny skin and loss of subcutaneous tissue in a denervated digit, marked transverse ridging or other irregularities of nail growth, and the presence of ulcers or their relics in the shape of scars

A variety of mechanical devices is available for the measurement of vasomotor activity The plethysmograph which measures blood flow is the most accurate method for determining the total circulation to a portion of a limb The method used by most observers both in this country and in America is based upon that originally devised by Hewlett and van Zwaluwenburg (1910) By this method, valuable information has been obtained about the circulation to the forearm and hand (Lewis and Grant, 1925), the forearm and calf (Grant and Pearson, 1938 , Wilkins and Eichna, 1941 , Abramson, 1944), the hand (Freeman, 1935), and the digits (Bolton *et al*, 1936 , Wilkins *et al*, 1938) Recently Hertzmann (1938) has described a photo-electric plethysmograph which is undoubtedly the most sensitive and accurate apparatus yet devised for the study not only of vasomotor activity in the cutaneous blood vessels, but also that in individual arteries which are near the surface, such as the radial, metacarpal and digital vessels (Hertzmann and Dillon, 1940 , Hertzmann, 1941) Of the more indirect methods two require mention The elimination of heat from the surface of a limb may be measured calorimetrically, and this method was adopted by Stewart (1911) Stewart believed that from data obtained in this way the blood flow to an extremity could be calculated, but Sheard (1926) has shown that the number of variables involved is too great for accurate results to be obtained The method can be used for demonstrating gross vasomotor changes such as those following sympathectomy or in cases of advanced peripheral vascular disease (Kegerreis, 1926 , Brown, 1926) It is, however, a cumbersome and time-consuming method which requires elaborate apparatus and is incapable of following rapid alterations in vasomotor activity The remaining method is the recording of skin temperature [1] Since this is the method adopted for the present study, it will be considered in some detail

The temperature of an area of skin at any given time is the resultant of the heat brought to it by the blood stream and the heat lost from its surface Heat loss from the skin surface is accomplished chiefly by radiation, the skin behaving approximately as a black body in this respect If the external factors governing heat loss (the environment) remain relatively constant, it is reasonable to assume that a rise in skin temperature represents an increase in blood flow (vasodilatation), and a fall in skin temperature a decreased blood flow (vasoconstriction) in the cutaneous blood vessels At the extremes of vasoconstriction and vasodilatation skin temperature will not be a reliable index of blood flow Once skin temperature approximates to environmental temperature, further vasoconstriction will not be accompanied by an appreciable fall in skin temperature At the opposite extreme there is a maximal value (35 36°C) for skin temperature , once this level is reached any further increase

1 Autonomic activity may also be studied by the electrical measurement of skin resistance, but since this is dependent upon sudomotor as well as vasomotor activity it is not considered here

in blood flow cannot be recorded by readings of skin temperature As an example of the relationship between skin temperature and blood flow, Lewis (1924) quotes the case of a patient with a traumatic arteriovenous fistula in whom closure of the fistula increased blood flow to the hand by 100 per cent and raised skin temperature from 33 to 33 5°C , *i e* at this high skin temperature an increase of 0 5 C is equivalent to a twofold increase in blood flow Wright and Phelps (1940) state that a blood flow of 2 c c per 100 c c of tissue per minute is sufficient to maintain a skin temperature of 32-33 C An increase from 3 c c per 100 c c per minute to 10 c c per 100 c c per minute may be accompanied by a rise in skin temperature of only 1°C These examples indicate that at high skin temperatures minor fluctuations may be of considerable significance

A rough estimate of the temperature of the skin may be made by palpation As Lewis (1936) points out, the skin of the dorsal surface of the middle phalanx of a finger is the most sensitive indicator It must be realised that temperatures within a range of 5 C on either side of the skin temperature of the examining digit will not be appreciated as either warm or cold (Trotter and Davies, 1909) Therefore, if the observer has an approximate idea of the skin temperature of his own finger under the environmental conditions of the examination, it is possible for him to give a rough estimate of the temperature of the part examined

For accurate estimations some form of apparatus is essential[1] Mercury-in-glass thermometers similar to ordinary clinical thermometers will provide fairly accurate readings but have many disadvantages They can be applied to only one area of skin at a time and must be left in situ for several minutes before a reading is obtained A certain amount of pressure must be exerted to obtain good apposition of the thermometer bulb to the skin Since only one side of the bulb is in contact with the skin and the other is exposed to the air or covered with adhesive strapping, the temperature recorded will be lower than true skin temperature This type of thermometer was used by Davy (1814) who overcame one difficulty by fixing the bulb of the thermometer to a small piece of cork lined with wool so that half of the bulb was applied to the skin and the other half was adequately insulated Other early and accurate observations on skin temperature recorded by mercury thermometers are to be found in the writings of Waller (1861-62), Hutchinson (1866), and Ogle (1869) Campbell and Angus (1928) also used a thermometer of this type and advocate that the bulb should be rolled over the skin so that the whole surface is in contact during the time necessary to obtain a reading Ipsen (1929) used mercury-in glass thermometers which he applied to skin covered by a layer of felt His procedure is as follows a layer of felt 5 cm square is applied to the skin for 10-15 minutes the thermometer bulb is then inserted under the felt and after a few minutes a reading taken He claims that temperatures so obtained represent true skin temperature and not the resultant of skin and air temperature , the bulb of the thermometer lies in an insulated layer where blood is circulating, and the influence of the evaporation of moisture is eliminated by the presence of the felt Stewart

[1] For a detailed account of the factors which influence skin temperature and the methods of measurement see the review by Murlin (1939)

(1930) suggests the routine use of an ordinary one-minute clinical thermometer for reading skin temperature Like Davy, he describes a method of insulating two-thirds of the circumference of the bulb so that only the surface which is to be placed in contact with the skin is exposed This is then applied to the skin for two to three minutes until the mercury stops rising There is no doubt that, if correctly used, a mercury thermometer will give results for resting skin temperature comparable with those obtained by more elaborate apparatus, but the method is obviously unsuitable for recording fluctuations in vasomotor activity

The earliest mechanical device utilised for measuring skin temperature appears to have been "the thermo-electric disks of M Becquerel,"[1] which were used by Weir Mitchell and his colleagues (1864) for the study of temperature changes after gunshot wounds of peripheral nerves Benedict and his co workers (1919 and 1928) used a thermocouple composed of a copper-constantan junction enclosed in a special insulated holder This can be held in the hand and the junction applied to and drawn firmly across the surface of the skin The copper and constantan wires are connected to a sensitive galvanometer and the circuit completed by a similar thermocouple immersed in water in a thermos flask, the temperature of which is maintained constant at 32°C by a thermostat When the circuit is complete, the galvanometer deflection will be proportional to the difference in temperature between the two thermocouples Since one temperature is maintained constant, it is possible to calibrate the galvanometer so that it will read the temperature of the thermocouple applied to the skin directly in degrees centigrade or fahrenheit Results obtained with this apparatus were very accurate and were rapidly obtained so that with a self-recording galvanometer it was possible to draw the junction over the skin and obtain a curve representing the skin temperature of a number of points on the body surface Bedford and Warner (1934), who made a critical analysis of methods of recording skin temperature, found that readings made by this type of junction were influenced to a certain extent by the temperature of the observer's hand

A similar type of apparatus was used by Lewis (1927) for the measurement of skin temperature, and most thermocouple circuits are designed on this principle For the constant temperature junction, ice and water in a thermos flask is commonly used, as such a mixture will maintain a constant temperature of 0°C for long periods The apparatus used in the present study (Figs 3 and 4) is a more elaborate modification of Lewis's original apparatus described by Grant (1935)[2] It consists of six copper-constantan thermocouples connected in parallel to a sensitive galvanometer To avoid the necessity for obtaining ice and water each time the machine is used, the cold junction is contained in a thermos flask without ice and water, so that although fluctuations in room temperature affect it to a certain extent, it will maintain a constant temperature for long periods The machine requires to be calibrated each time it is used by setting the "zero" of the galvanometer to correspond with the temperature of the cold junction and balancing it with the variable resistance provided in the machine The apparatus is portable and adjustment requires only a few

[1] These were described by Becquerel and Breschet as early as 1838

[2] Supplied by the Cambridge Instrument Company

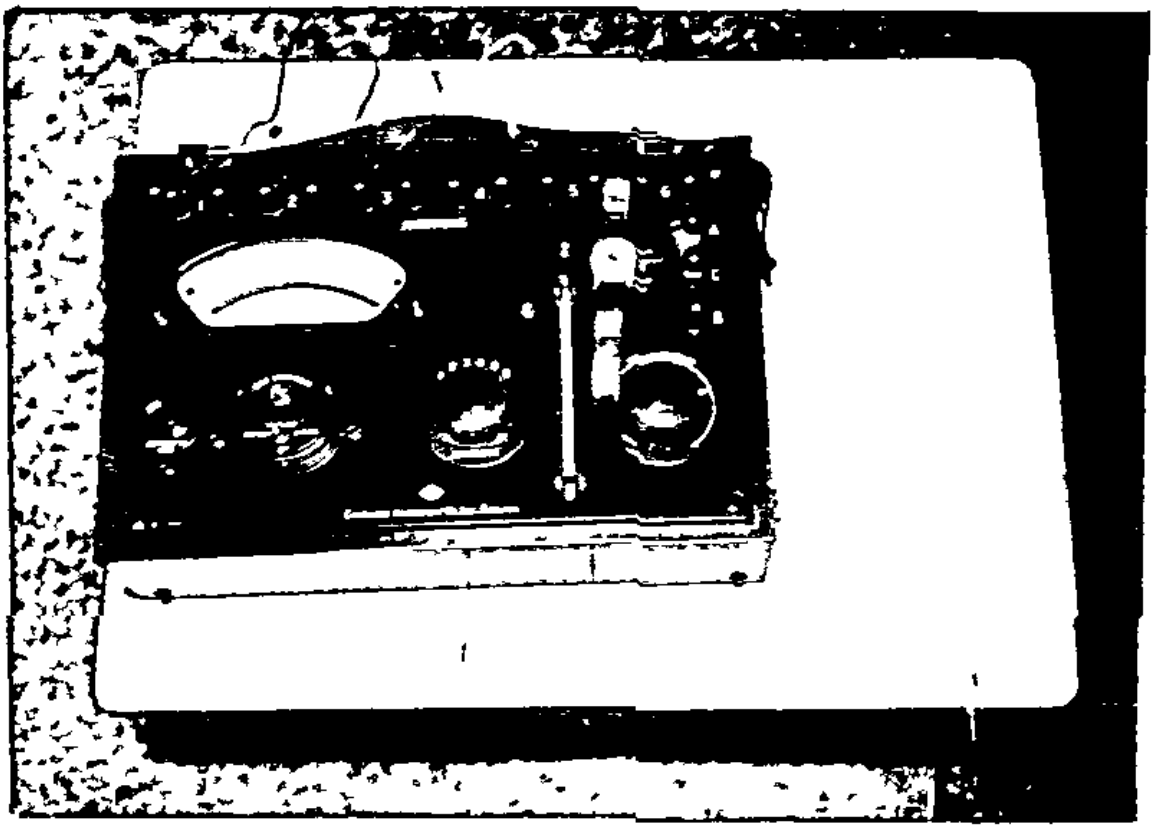

FIG 3
Apparatus for measuring skin temperature

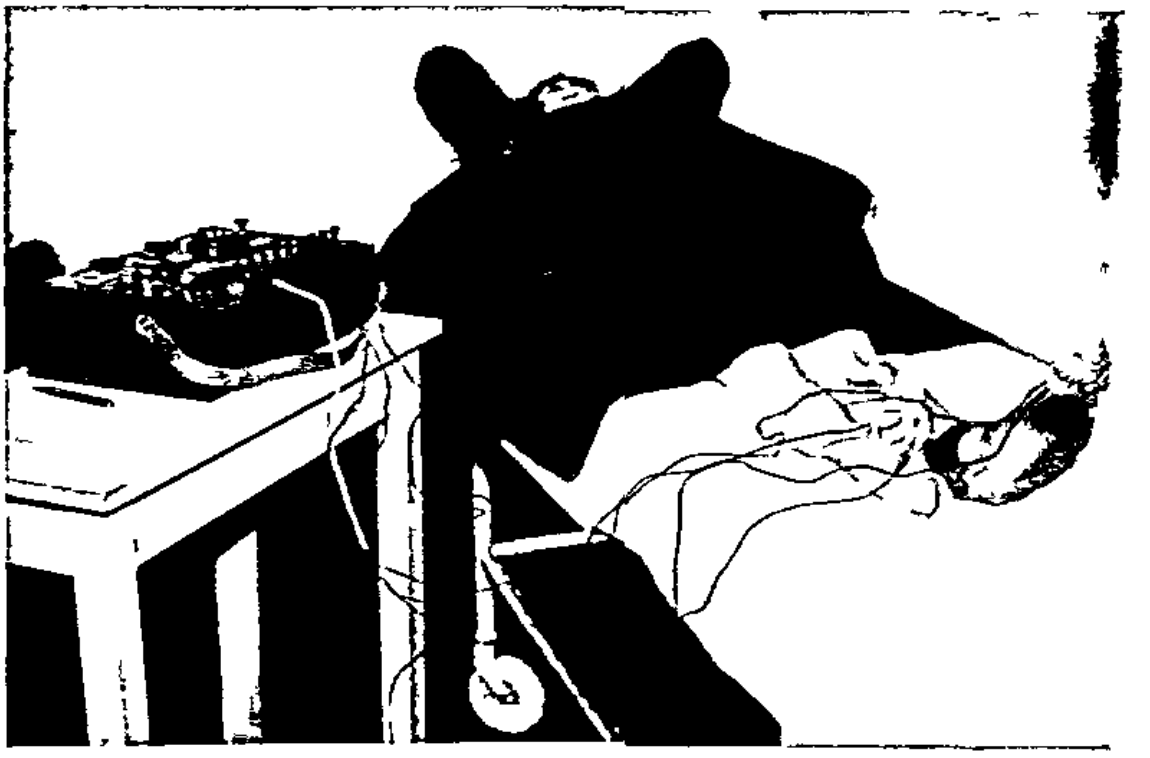

FIG 4
Apparatus in use

minutes The galvanometer scale is calibrated directly in degrees centigrade and allows accurate readings to 0 25°C The six thermocouples can be switched into the circuit one after another, and since the galvanometer responds fairly rapidly, it is possible to measure the temperature of six different points within a matter of two to three minutes The thermocouples are completed by twisting the bare ends of the copper and constantan wires together for a distance of about half an inch, and soldering them These thermocouples are attached to the skin by strips of adhesive tape It will be readily appreciated that there are certain disadvantages even to this type of apparatus The area of skin under observation is covered by adhesive tape On fleshy areas such as the thigh it is sometimes difficult to obtain good apposition between the thermocouple and the skin, while on others, particularly the digits, there is a danger that the strapping, by pressure or constriction, might interfere with the circulation and thus give rise to incorrect readings The only type of skin temperature apparatus in which these difficulties are overcome is the radiation thermopile Comparing results obtained by various types of apparatus with those obtained by a thermopile, Bedford and Warner (1934) conclude " Of the types of thermojunction tested by us the simple Lewis type of junction attached and protected by a strip of surgical tape appears to give the most accurate results The average error taking the thermopile values as standard was only 0 5-0 8°C and the thermojunction temperatures were consistently higher than the thermopile values by about this amount " It may therefore be assumed that the results obtained are accurate to within 1°C Since the tests of vasomotor activity which have been used all cause considerable fluctuations in skin temperature, this degree of accuracy is considered sufficient Details of the various vasomotor tests will be given when discussing vasomotor activity in normal limbs

SUMMARY

Methods applicable to the recording of vasomotor activity in the limbs of man are discussed The importance of clinical examination is stressed The measurement of skin temperature is considered and the apparatus used in the present study described It is considered that results obtained by this apparatus are sufficiently accurate for the present purpose

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CHAPTER THREE

SPONTANEOUS VARIATIONS IN VASOMOTOR ACTIVITY

IN health the relative constancy of the internal temperature of the human body is an indicator of the efficiency of its thermo regulatory mechanism Heat production must fluctuate considerably according to the body's different metabolic needs , it follows that body temperature must be kept constant by a corresponding variation in the amount of heat loss Heat is lost from the body surface in two main ways by radiation of heat from the skin (76 per cent) and by the evaporation of moisture (24 per cent) The temperature of the skin at any given time represents the balance between the heat which is being brought to it by the blood stream and that which is being lost from its surface by the processes of heat dissipation While the whole surface of the body plays a part in the heat regulating mechanism, the limbs, by virtue of their relatively large surface area, play the major role In fact it is found that although the limbs account for 65 per cent of the surface area of the body, they are responsible for 75 per cent of the heat loss which occurs under normal environmental conditions (Loewi, 1914) This important function of the limbs in the regulation of body temperature is the most important factor in determining their vasomotor state at any given time

1. THE INFLUENCE OF ENVIRONMENTAL TEMPERATURE

If the body is exposed at a relatively comfortable environmental temperature (20 23°C) for a period long enough for equilibrium to be established and the temperature of the skin recorded thereafter, it is found that the highest temperatures are recorded over the face and trunk and the lowest at the extremities , the fingers as a rule being a degree or two warmer than the toes (Benedict *et al* , 1919 , Talbot, 1931 , Coller and Maddock, 1932) In response to alterations in environmental temperature it is found that, unless the temperatures are extreme, the surface temperature of the face and trunk tends to remain constant and heat is conserved or lost as the case may be by vasoconstriction or vasodilatation, represented by a fall or rise in the skin temperature of the extremities The face temperature in particular is remarkably constant under varying environmental conditions, and is regarded by Benedict and his co workers as being a peculiarity of the individual (Benedict and Parmenter, 1928) It is found (Benedict *et al*, 1919) that if a curve be drawn representing the skin temperature of the points on a line drawn from the mid point of the clavicle to the foot, the difference between the highest (waist) and lowest (foot) points of the curve at an environmental temperature of 16 4°C is 10 6°C , whereas at 30°C the difference is only 4 2°C This flattening out of the curve is the result

of the approximation of the lower temperatures to the higher ones which remain relatively constant Maddock and Coller (1933) observe that in response to an increase in environmental temperature from 25°C to 34°C, the greatest rise in temperature occurs in the lower limbs, and particularly in the toes The influence of a low environmental temperature was studied by Freeman and Nickerson (1938) Exposure of the body to an environmental temperature of 20°C or 15°C for a period of 2 hours results in a rapid fall in skin temperature during the first hour and a more gradual fall during the second hour The greatest fall in temperature is observed in the toes and the least in the forehead, which may even show a slight rise At 15°C the fall in skin temperature is more precipitate and the ultimate temperatures are lower than at 20°C

More recent work carried out by Sheard and his colleagues at the Mayo Clinic (Sheard *et al*, 1938 and 1941, Roth *et al*, 1940) has further elucidated the role played by the extremities in the conservation and dissipation of heat under different environmental conditions These workers find that at environmental temperatures from 18 to 22°C the temperature of the toes remains at or near atmospheric temperature As the temperature rises through this range, however, the temperature of the fingers gradually rises until they reach full vasodilatation (33-35°C) Once this level is reached, the temperature of the toes begins to exceed atmospheric temperature and continues to rise until they also have reached maximal vasodilatation This occurs at environmental temperatures in the neighbourhood of 28-29°C Above this level the temperature of fingers and toes is similar Any further heat loss in response to a still greater rise in environmental temperature is accompanied by maximal generalised vasodilatation which occurs at about 30°C Above this level heat loss can be accomplished only by the evaporation of moisture and profuse sweating occurs It should be noted that skin temperature is relatively little affected by alterations in the relative humidity of the atmosphere

From these data it will be observed that there is a range of environmental temperature from 18 to 22°C through which, since the vasomotor regulation of heat loss is being controlled by the hands, the temperature of the lower limbs may be expected to remain relatively constant within narrow limits If within this temperature range observations are made on the skin temperature of the lower limbs from *groin to toes it is found that there is a progressive fall in temperature from the* proximal to the distal portion of the limbs The term "vasoconstrictor gradient" with reference to this progressive fall in temperature was first used by Morton and Scott (1931) A similar finding was noted by Eddy and Taylor (1931) who made observations on the resting skin temperatures of 50 healthy medical students at a room temperature of 20°C They observed that the gradient tended to be steeper in slender individuals with a tendency to cyanosis of the extremities Foged (1932) also remarked upon the presence of a gradual fall in temperature in the lower limb between hip and foot, age, sex and prolonged recumbency did not appear to influence the gradient, but those with long legs showed a considerably lower temperature at the periphery Coller and Maddock (1932) noted that there was also a

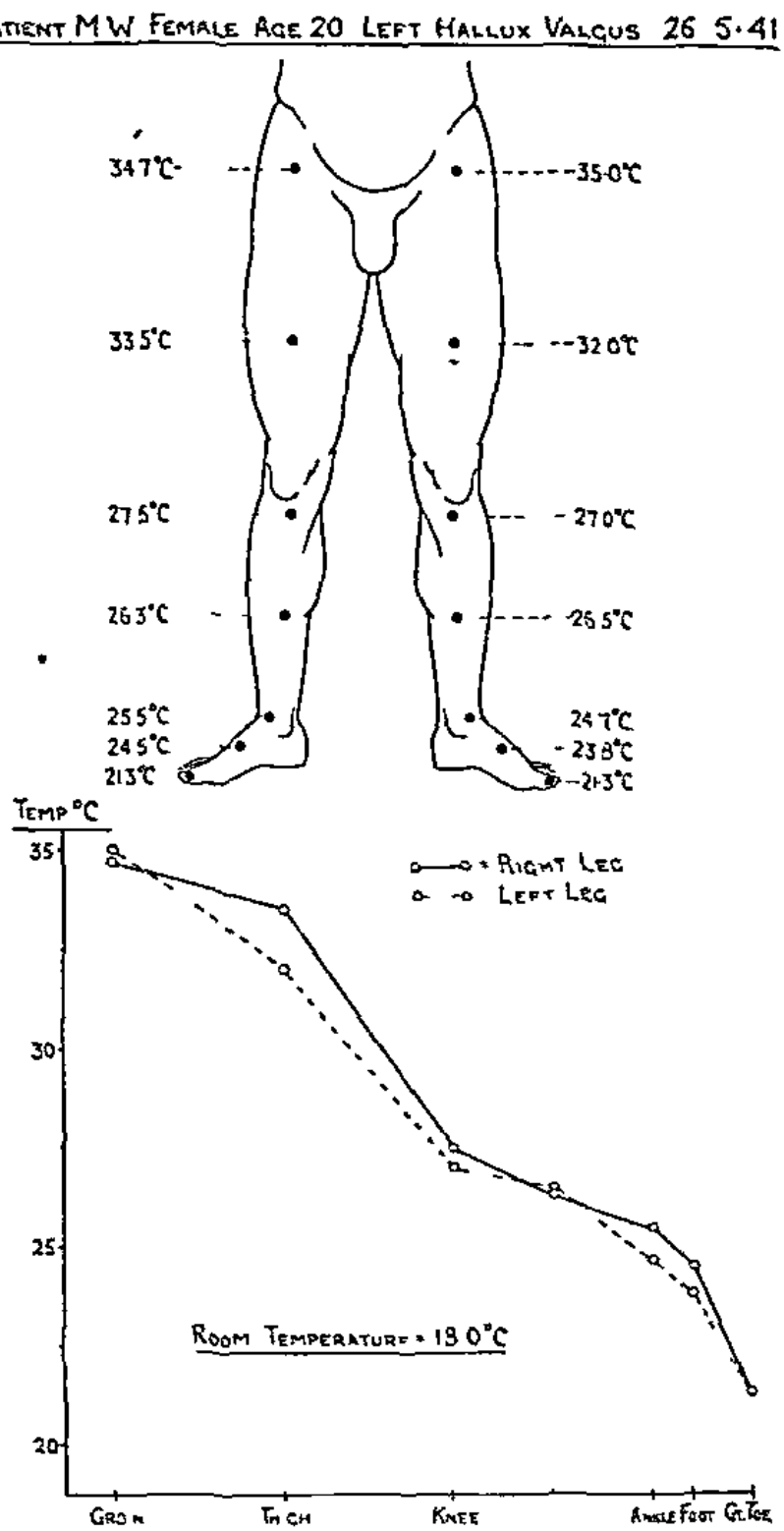
tendency for a slight gradient to be present in the digits, the temperature falling slightly from great toe to little toe

Normally there is a striking bilateral symmetry of skin temperature A very slight tendency for the limbs on the right and the trunk on the left to be warmer was noted by Freeman *et al* (1937) Ipsen (1929) and Coller and Maddock (1932) observed that any slight differences were usually noted in the toes For practical purposes these differences are insignificant and if any vasomotor test is to be performed on one limb the corresponding limb may safely be used as a satisfactory control

The work referred to so far has been carried out in America where the prevailing indoor environmental temperatures are somewhat higher than those in this country In a study of the skin temperature of several thousand factory workers made while they were clothed and engaged at their normal duties, Bedford (1935) found that at an air temperature of 18°C the average skin temperatures were as follows forehead 34 25°C, palm of hand 29 2°C, foot 24°C, the variations being 0 81°C for the forehead, 2 51°C for the hand and 2 80°C for the foot

At the outset of the present study a number of observations were made on the resting skin temperature of the lower limbs in a series of " normal " patients Those selected had been admitted to hospital for conditions other than those affecting the cardiovascular system Both sexes were represented and the ages ranged from 7 to 75 years The procedure adopted was as follows —

The patient lay on a bed with the lower limbs exposed for at least 30 minutes before any observations were made From the experience of Freeman and Linder (1934) this period was perhaps rather short for an equilibrium between skin and environmental temperature to be reached In practice, however, it was usually found adequate and it was a simple matter to decide at the initial readings whether such an equilibrium had been attained At least one hour was allowed to elapse after a meal before the test was commenced This was quite sufficient because (as will be explained later) the ingestion of food has little effect on the skin temperature of the lower limbs at the environmental temperatures used Corresponding points on the two lower limbs were marked and thermocouples attached to these Since the apparatus used carried only six thermocouples and at least six points on each limb were selected, it was not possible to record readings at all points simultaneously As a rule the three most proximal readings were recorded first Three readings at intervals of approximately two minutes were taken from each point If these differed by more than 0 5°C, further readings were made until a satisfactory equilibrium had been established The thermocouples were then moved distally and the procedure repeated The results were recorded on a special chart and from these a graph could be drawn if considered necessary (Fig 5) A room of constant temperature was not available and the room temperatures in the series varied from 18 to 22°C These temperatures were not preselected, and may be considered as average indoor environmental temperatures for this country It will be noted that the range corresponds to that within which the temperature of the lower limbs is expected to remain relatively constant



READINGS RECORDED AFTER 40 MINUTES EXPOSURE OF LIMBS AT ROOM TEMPERATURE OF 18°CENTIGRADE

FEET RATHER PALE IN COLOUR AND FEEL COLD BUT ARE SIMILAR IN TEMPERATURE TO THE TOUCH

PULSES PERIPHERAL PULSES OF GOOD VOLUME IN BOTH FEET

LEGS – SOMEWHAT "MARBLED IN APPEARANCE

FIG 5

Skin temperature observations normal lower limbs, to show method of recording.

The results in 30 cases are summarised in the accompanying table (Table I) and in Fig 6

TABLE I

Skin Temperature Observations in Lower Limbs

Results in 30 Cases. Room Temperature 18-22°C.

	Temperatures—Degrees Centigrade					
	Right Leg			Left Leg		
	Max	Min	Average	Max	Min	Average
Groin	36 5	30 5	33 4	36 3	30 5	33 5
Mid thigh	33 5	28 5	30 7	33 3	28 2	31
Knee	31	25 8	28 2	31 3	25 6	28
Ankle	30 2	22 8	27 3	28 5	22	25 5
Dorsum of Foot	28 5	19 7	24 5	27 5	20 7	24 1
Great Toe	28 7	16 8	20 3	23 7	16	20 3

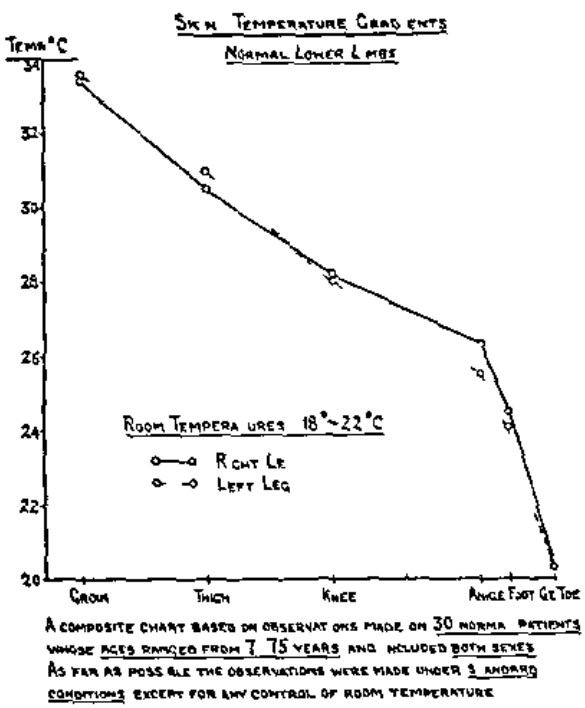


FIG 6
Vasoconstrictor gradient in normal lower limbs Data from Table I

The progressive fall in temperature from the groin to the toes will be noted, and also the small difference between the results for the two limbs A steady gradient such as that illustrated in the graph (Fig 6) was not observed in every case it was frequently observed that the knee was colder than the calf or ankle Minor differences between corresponding points in the two limbs were common but differences of more than 1°C were uncommon The greatest difference in any one case was observed in a girl aged 9 years where there was a difference of 6°C between the two great toes, no adequate explanation for this could be found Age and sex did not appear to influence the temperature gradient, although Coller and Maddock (1932) found that it was more pronounced in women than in men If the temperature gradient is

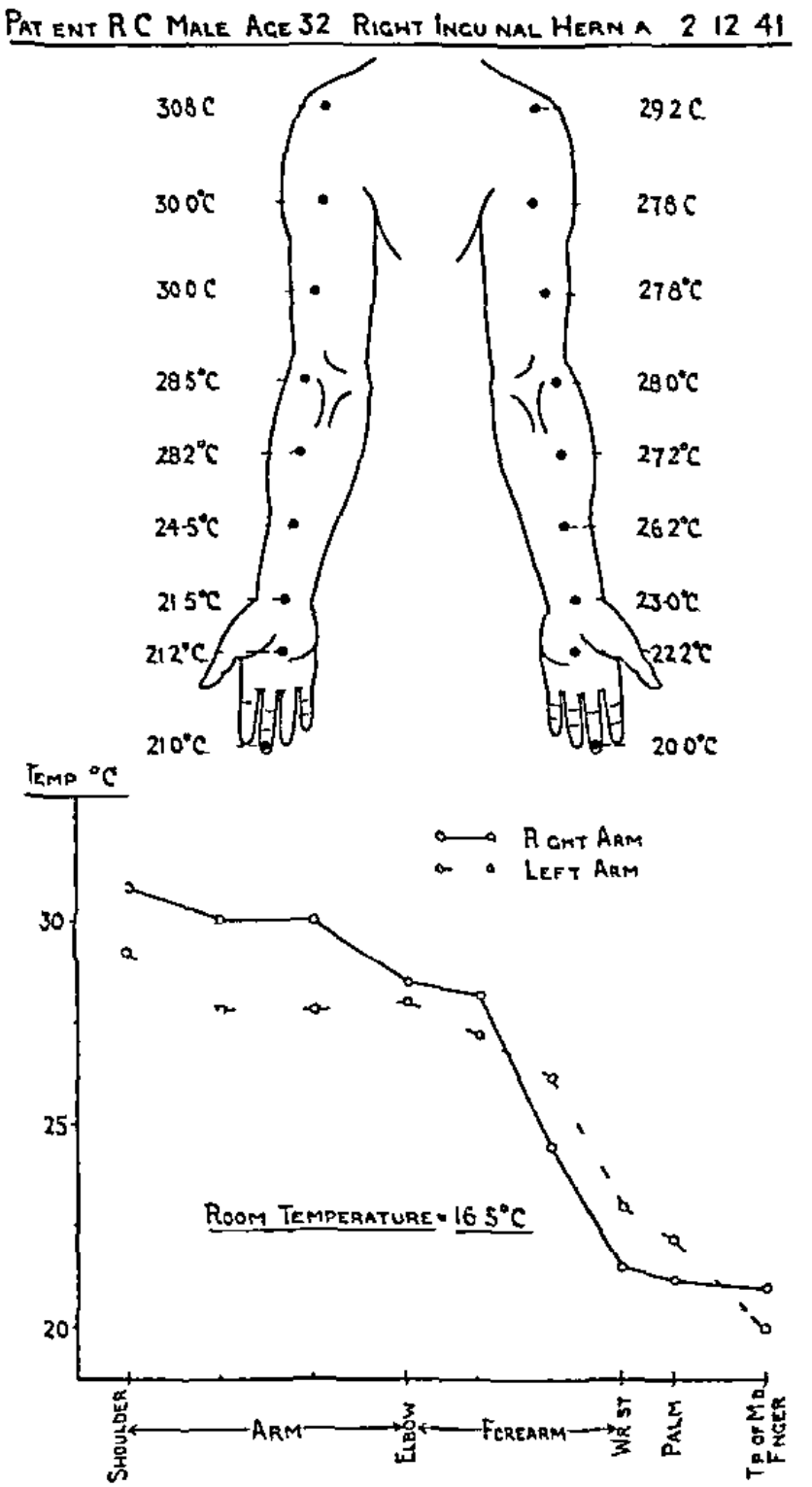


FIG 7

Skin temperature observations normal upper limbs

considered in relation to the length of the limb, there is relatively a much greater fall in temperature in the peripheral part of the limb In the present series of cases the average fall in temperature between the knee and ankle is 1 7°C , whereas that between the dorsum of the foot and the nail bed of the great toe is 4°C

It is more difficult to obtain corresponding observations on the upper limbs Wide fluctuations in temperature, particularly in the fingers, are observed as the result of even slight changes in environmental temperature, so that it is much more difficult to obtain standard temperature readings Individual variation in the temperature of the hands is also more frequent than in the feet It is a familiar clinical observation that the hands of those who have to work out of doors in all weathers (for example, fishermen and labourers) are frequently persistently cyanosed and cold to the touch, while those whose work is indoors (for example, professional men) tend to be warm-handed At temperatures in the neighbourhood of 15-18°C , a vasomotor gradient from mid-forearm to finger tips is frequently observed (Fig 7) Recently White and Smithwick (1942) have shown that by studying this gradient, individuals may be divided into two groups according to whether they are warm handed or cold handed It is probable that only a slight difference in degree exists between a normal cold handed individual and one who may be judged to be suffering from pathological peripheral vasospasm Under normal indoor environmental conditions such as prevail in this country, the unprotected hands are usually warm or cool as opposed to the feet which are cold These observations have a practical application in the heating of factories, schools and offices

2. RESPONSE TO ALTERATIONS IN METABOLISM

Increased metabolism means increased heat production Consequently, in order to maintain the constancy of the internal temperature of the body, there will be an increase in heat loss This is brought about by a greater diversion of blood to the skin surface which results in a raised skin temperature Maddock and Coller (1933) found that as a result of increased heat production (subjects were chosen with naturally or artificially raised basal metabolic rates) the increase in the skin temperature in the extremities was greater than that in the trunk Sheard *et al* (1941) found that under basal conditions (environmental temperature 25°C , relative humidity 40 per cent) the temperature of the toes was higher in those with a raised basal metabolic rate In cases of thyrotoxicosis the temperature of the toes tended to fall after treatment with Lugol s iodine or following thyroidectomy The temperature of other areas showed little relation to heat production, except for a slight correlation in the fingers and lower forearms It is a frequent clinical observation that those who have a low basal metabolic rate tend to have a sluggish peripheral circulation with cold, cyanosed extremities Cretins have a low skin temperature which can be elevated by the administration of thyroid extract (Talbot 1931)

Fasting results in a general lowering of both body and skin temperature (Talbot 1931) Following the ingestion of food, heat is at first stored within the body and there is a slight rise in body temperature After a short latent period the surface temperature rises more rapidly than the rectal temperature and the excess heat is

lost (Burton and Murlin, 1935) As a result, it is to be expected that the skin temperature of the extremities will rise after a meal The effect of the ingestion of food upon the peripheral circulation has been studied by Ingram (1936), Booth and Strang (1936), Roth *et al* (1938) and Abramson (1944) Ingram found that the ingestion of food did not have a constant effect upon the skin temperature of the hand and foot A small hot meal might cause a rise in temperature in the hand but did not always do so A larger meal less often caused a rise in temperature in the hand , this he attributed to diversion of blood from the surface to the splanchnic vessels He noted that the ingestion of food caused only a very slight rise in the temperature of the foot Booth and Strang found that a protein meal sufficient to produce a sensation of satiety caused a rise in temperature in the extremities which commenced 10 minutes after the meal and attained a maximum elevation of 2°C in 60 minutes , the response was delayed and diminished in obese patients A similar rise in the temperature of the extremities was noted by Roth *et al* Abramson observed that the increased blood flow to the viscera which accompanies digestion was not associated with a reduction in blood flow in the extremities Any change which did occur in the latter was in the direction of vasodilatation and was greater after a protein meal than after the ingestion of carbohydrate or fat He suggested that this might be due to vasodilator metabolites resulting from the breakdown of protein

These findings are somewhat conflicting but may be explained by reference to the environmental temperature The observations, with the exception of those made by Ingram, were recorded at high room temperatures (25-28°C) At such temperatures a relatively high degree of peripheral vasodilatation is already present , the hands will be approaching full vasodilatation and the feet will be warm Any further heat loss must be effected by a further rise in skin temperature, which will be greatest in the toes Ingram's observations were made at considerably lower environmental temperatures (15-20°C), and at this level the vasoconstrictor effect of cold was probably sufficient to mask the less pronounced effect of the ingestion of food This argument is confirmed by observations of Sheard *et al* (1941) who found that the ingestion of food at 20°C did not affect the temperature of the toes although it caused a rise in the temperature of fingers and lower arms

Exercise tends to raise body temperature by increasing heat production, but at the same time results in a diversion of blood from the surface to the muscles The studies of Benedict and Parmenter (1928) showed that during and immediately after exercise there is a slight but appreciable fall in skin temperature over the whole body, including the extremities It is interesting to note that this fall in temperature was observed even in cases where the subjects felt subjectively considerably warmer after the exercise

A so far unexplained vasomotor disturbance which is probably related to altered metabolism is the peripheral vasodilatation which is occasionally observed in cases of carcinoma and other diseases associated with severe cachexia (Morton and Scott, 1931)

3. EFFECT OF POSTURE

Alterations in the posture of the limbs have been observed to cause skin temperature changes in the fingers and toes. Roth *et al* (1938) and Sheard *et al* (1941) noted that elevation of the hands or feet caused a fall in peripheral temperature, while standing usually, but not invariably, caused a rise. If the muscular effort of standing was eliminated by having the patient on a tilting table and placing him in the feet down position, the rise in temperature was still observed. Youmans *et al* (1935) and Mayerson and Toth (1939) have reported contradictory results. According to these observers assumption of the erect posture was followed by a prompt and significant fall in the temperature of the toes. The greatest fall in temperature occurred during the first 15 minutes, but in some cases the temperature continued to fall all the time the patient was upright. Mayerson and Toth noted that full vasodilatation did not inhibit this vasoconstrictor response, but if active vasodilatation were taking place when the erect posture was assumed, then the vasoconstriction might be masked. Standing reduces the speed of blood flow to the lower limbs (Kvale and Allen, 1939). Neilsen *et al* (1939) found that a passive alteration in posture to the vertical caused general vasoconstriction except in the case of the toes in which there was a rise of temperature. They suggest that this dissociated response is a local protective mechanism to prevent undue cooling of the toes. As it was observed at high environmental temperatures and with toe temperatures in the region of 35-36°C., this appears somewhat unlikely. The rise or fall in digital temperature is never more than 1-2°C. In the present study the fluctuations in temperature upon which conclusions are based have always been greater than 5°C. During the performance of a vasomotor test, the patient has been allowed to rest the limb in the position of greatest comfort.

4. SLEEP

Kirk (1931) and Ingram (1936) observed that during sleep maximal peripheral vasodilatation occurred in both upper and lower limbs. The onset of the vasodilatation usually preceded the onset of sleep for the night by a period varying from 30 minutes to 2 hours. Vasodilatation persisted so long as deep sleep continued, but there was a fall even during short periods of wakefulness, and the temperature always became unstable for a period before awakening in the morning. This observation has been used occasionally in the present study as a simple test of the capacity of the vessels in a limb to dilate.

5. THE ROLE OF THE SYMPATHETIC

The regulation of body temperature is a function of the autonomic nervous system. The distribution of sympathetic nerve fibres to the limbs has been shown to be predominantly peripheral. It is, therefore, not surprising that, in response to the physiological needs of the body, the greatest fluctuations in surface temperature should take place in the extremities. Under normal environmental conditions the vasoconstrictor gradient observed in the lower limbs, and to a lesser extent in the

upper limbs, is the result of a continuous " vasoconstrictor tone " which is imposed upon the cutaneous blood vessels by the sympathetic Depending upon the needs of the body for the conservation or dissipation of heat, the degree of this " tone " is varied so as to produce increased vasoconstriction or vasodilatation

It is necessary to consider what is meant by the term " vasoconstrictor tone " The work of Adrian and Bronk has shown that efferent sympathetic nerve fibres carry persistent electrical discharges which are chiefly concerned with vasoconstriction (Adrian *et al*, 1932, Bronk, 1934) The frequency of these discharges is not constant but is continually fluctuating in an intermittent but rhythmic manner With a skin temperature apparatus such as that used in the present study, the temperature of an area of skin may be found to remain constant for very long periods, and there is little evidence of fluctuations in vasomotor activity such as would be expected as a result of these fluctuations in sympathetic activity If the more sensitive plethysmograph is used, however, it is found that there is a great physiological variability in the blood flow to the digits at rest (Burton, 1939 and 1941, Burton and Taylor, 1940) Some of the fluctuations in blood flow are related to alterations in respiration and blood pressure, but when these are excluded there remain other fluctuations which can be attributed only to fluctuations in sympathetic activity These rhythmic fluctuations in the blood flow to the digit at rest are found to be greatest when the blood vessels are in a state between vasoconstriction and vasodilatation At full vasoconstriction and full vasodilatation the fluctuations are minimal Using the photo electric plethysmograph, Hertzmann and Dillon (1939) have shown that these spontaneous fluctuations in vasomotor activity are not confined to the digits but may be observed all over the skin surface and in the nasal septum It is thus possible to postulate a nervous control of the cutaneous blood vessels of the following nature When the need is for heat conservation frequent bursts of impulses are passing along sympathetic vasoconstrictor fibres Since the response of the sympathetic effector organs is comparatively slow (Adrian *et al*, 1932), this is sufficient to maintain continuous constriction of the cutaneous vessels At the other extreme, few impulses are passing, vasodilatation is favoured, and heat is lost relatively rapidly In the mid zone there is a continuous rhythmic fluctuation in cutaneous blood flow which, however, has little effect on the so-called " resting " skin temperature This hypothesis has the merit that it is based upon the activity of vasoconstrictor fibres only, and does not postulate the presence of vasodilator fibres whose existence is still somewhat problematical (p 12)

The vasomotor centre varies the frequency and rhythm of the sympathetic discharges in accordance with the needs of the body as a whole The origin of afferent stimuli reaching the centre which cause modifications of the efferent impulses is as yet uncertain Alterations in the temperature of the blood reaching the centre, or any chemical or hormonal mechanism, appear to be unlikely since the time lag in such a system would be too great to account for the rapid changes in blood flow which may be observed in the skin Afferent nervous impulses arising from temperature receptors disposed in depth in the skin appear to be more probable As Burton (1941) suggests, it seems more likely that the temperature gradient of the

skin from the surface to the deeper layers is the important factor rather than the absolute temperature of the skin surface This is not the full explanation, however, for spontaneous rhythmic fluctuations in the blood flow to the digits are present even when the whole body is immersed in a water bath at a constant and comfortable temperature (Burton and Taylor, 1940)

6. LOCAL FACTORS

Vasomotor activity in the limbs has so far been considered in relation to the needs of the body as a whole Local factors are also operative and must now be taken into consideration The amount of blood reaching any part of the body must be sufficient to meet the local metabolic needs, otherwise ischaemia or gangrene would result To anyone studying vasomotor activity in the limbs by skin temperature or other methods, it soon becomes evident that there is a fundamental difference between the more proximal portions of the limbs (forearm and leg) and the extremities (hand and foot) The vasomotor state of the former is more stable and fluctuates much less in response to environmental changes than does that of the latter The proximal segments of the limbs contain a relatively large volume of muscle, and Grant and Pearson (1938) have shown that the skin temperature of the forearm and calf is largely dependent upon the activity of the underlying muscle Plethysmographic studies show that the blood flow to forearm and calf is directly related to the local metabolic need, whereas, except at very low environmental temperatures, that to the hand and foot is commonly in excess of local needs because of the " safety valve " function which the extremities fulfil in the regulation of body temperature (Abramson *et al*, 1941) Although it has recently been shown that there is a certain amount of sympathetic vasoconstrictor tone in human skeletal muscle (Barcroft *et al*, 1943), the calibre of the blood vessels in the muscles is controlled chiefly by chemical metabolites produced by muscular activity (Grant, 1938) Unless the need for heat conservation or dissipation is extreme, the sympathetic exerts relatively little effect on the proximal portion of the limbs and their vasomotor state is determined chiefly by the local metabolism

A second local factor is the ability of blood vessels and particularly cutaneous blood vessels to respond directly to local changes in temperature Local cooling produces vasoconstriction and local warmth vasodilatation (Lewis, 1927) This local mechanism serves two useful functions it conserves heat when only a portion of a limb (for example, one hand) is exposed to a change in temperature, and it also increases or decreases local blood flow so as to cope with the alterations in metabolism which follow the local temperature change In the hand (Freeman, 1935) and in the fingers (Wilkins *et al*, 1938) the vasodilator effect of local heat is less than that of warming the body as a whole, that is, the effect of local heat is not sufficient to abolish entirely vasoconstrictor tone It has been suggested (Hyndman and Wolkin, 1941) that the local response of the cutaneous blood vessels to external thermal stimuli is the main regulating factor in the control of body temperature, and that the central mechanism functions only as a " governor," coming into play when the need is extreme or when it is necessary to utilise the whole skin surface in response to a

sudden change in the environmental temperature affecting only a part of the body surface From what is known of the activity of the autonomic nervous system in relation to other viscera which have smooth muscle in their walls, it appears more rational to assume that the central mechanism is normally predominant

SUMMARY

Vasomotor activity in the limbs may be studied by observations on skin temperature In response to the physiological needs of the body for the conservation or dissipation of heat, striking vasomotor changes are observed in normal limbs These changes are most pronounced in the extremities which play a relatively major role in the regulation of body temperature Environmental temperature is the chief factor controlling the skin temperature of the limbs, but the basal metabolic rate the ingestion of food exercise sleep and possibly alterations in posture are all contributory factors Under normal environmental conditions such as prevail in this country a vasoconstrictor gradient exists from proximal to distal in the lower, and to a less extent in the upper limbs This is the objective manifestation of sympathetic vasoconstrictor tone which is exerted chiefly upon the cutaneous blood vessels of the extremities The nervous mechanism involved in sympathetic vasoconstrictor tone is discussed In the more proximal portions of the limbs, local factors, particularly local metabolites, are more important than sympathetic activity

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CHAPTER FOUR

IMPOSED VARIATIONS IN VASOMOTOR ACTIVITY

IN the previous chapter alterations in vasomotor activity in the limbs in response to the physiological requirements of the body were considered It is now proposed to consider alterations in vasomotor activity which, when imposed upon a limb, provide information regarding the state of the peripheral circulation

1. RAISING BODY TEMPERATURE

It has already been stated that peripheral vasodilatation occurs in response to a rise in body temperature This observation formed the basis of the first practical method of testing the peripheral circulation in a limb Brown (1926) induced an artificial pyrexia by the injection of a foreign protein (typhoid vaccine), and measured the vasodilatation which occurred in the extremities during the period of reaction The rise in peripheral skin temperature and the rise in oral temperature were both recorded, and from these Brown calculated a factor which he called the " Vasomotor Index," viz. —

$$\text{Vasomotor Index} = \frac{\text{Rise of peripheral skin temp} - \text{Rise of mouth temp}}{\text{Rise of mouth temp}}$$

A high vasomotor index indicates a large element of vasospasm a low vasomotor index considerable vascular occlusion The test is at best only a qualitative one, and the pyrexia is exceedingly unpleasant for the patient Moreover in cases of peripheral vascular disease the method is not without danger since during the period of chill which precedes the rise in peripheral temperature severe vasoconstriction occurs which may even result in thrombosis in vessels already diseased (White and Smithwick, 1942) For these reasons this test has not been used in the present investigation

The body temperature may also be raised artificially by heating the trunk in a hot air bath with the extremities exposed (Fig 8) This method of inducing peripheral vasodilatation was used by Lewis

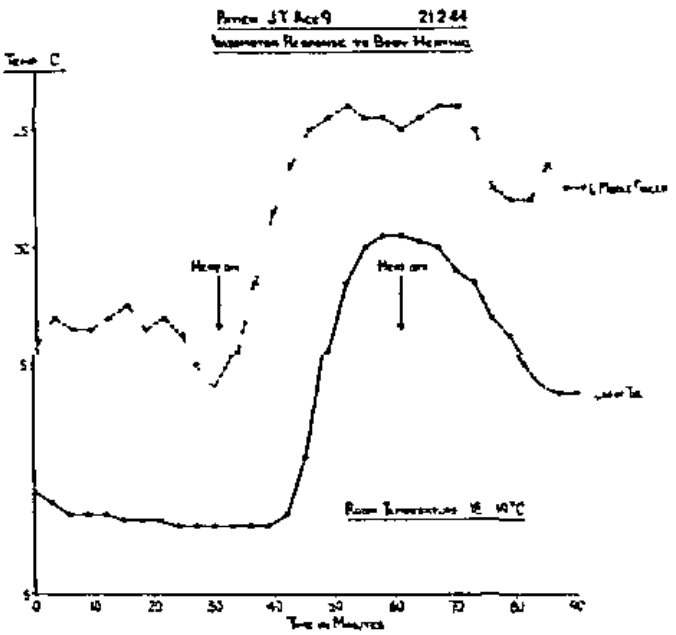

FIG 8
Peripheral vasodilatation in response to heating the trunk with a shock cage

and Pickering (1931), and has been studied more critically by Pickering and Hess (1933) and by Uprus *et al* (1935 and 1936) It is found that peripheral vasodilatation is normally preceded by a rise in blood temperature The degree of peripheral vasodilatation which occurs is dependent upon the local temperature of the extremity and its posture, and is always greater and occurs earlier in the hands than in the feet To anyone who is studying vasomotor activity in the limbs it is soon apparent that there are fundamental differences between the responses of the hands and feet It has already been mentioned that the feet are normally colder than the hands, and do not dilate so readily in response to a rise in environmental temperature Even when the initial temperature of fingers and toes is similar, vasodilatation in response to body heating always occurs more readily in the fingers This holds good even if the fingers are the site of pathological vasospasm (Horton *et al*, 1936) This difference in response of the fingers and toes is attributable to a greater intensity of normal vasoconstrictor tone in the lower extremities This is probably associated with the assumption of the erect posture, Doupe *et al* (1937) have shown that afferent impulses probably arising from receptors in the walls of the veins are partly responsible for maintaining an increased vasoconstrictor tone in the lower limbs It is probable that body heating causes in the upper limbs complete, in the lower limbs incomplete, relaxation of vasoconstrictor tone Exceptionally, vasodilatation in the feet may not follow body heating when the peripheral blood vessels are normal (cf Fig 12) In such cases if the temperature of the feet is initially raised to a slightly warmer level (24 25°C), a normal response may be obtained

This method of the hot air bath is not entirely satisfactory Only a low gradient of blood temperature rise is induced and, unless blood temperature is rising rapidly, a failure to respond, particularly in the lower limbs, does not necessarily indicate any structural disease of the peripheral vasomotor mechanism (Uprus *et al*, 1936) One advantage of the method is that by the use of a radiant heat cage it can be applied to bed-ridden patients, and for this reason it has been used occasionally in the present study For other patients alternative methods have been preferred

2. REFLEX VASODILATATION AND VASOCONSTRICTION

Under suitable circumstances the application of heat or cold to an extremity will produce reflex vasomotor effects in the other extremities Brown-Sequard and Tholozan (1858) observed that lowering the temperature of one hand by immersing it in ice and water resulted in a considerable lowering of the temperature of the other hand without any appreciable lowering of body temperature Sewall and Sanford (1890) showed that plunging one forearm and hand into ice-cold water and water at 48°C caused a reduction and an increase respectively in the volume of the opposite forearm and hand This they attributed to reflex vasoconstriction and vasodilatation Stewart (1911) investigated these responses by heat elimination studies in a calorimeter, and showed that, while cooling one hand was followed immediately by a reduction in blood flow in the other, there was an appreciable delay between the application of heat and the occurrence of reflex vasodilatation

Gibbon and Landis (1932) studied the vasodilatation in the toes in response to the immersion of the arms in hot water, and showed that this could be used as a clinical test of vasomotor activity

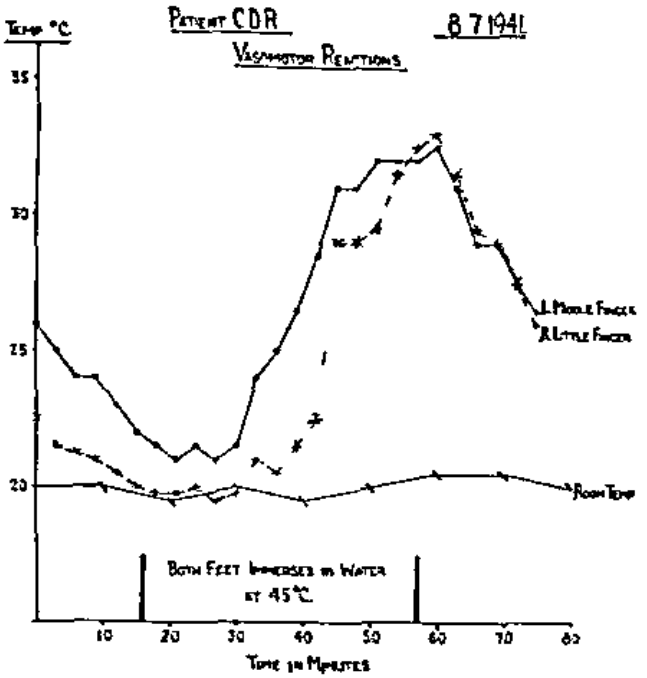

FIG 9
Upper limbs—normal reflex vasodilatation

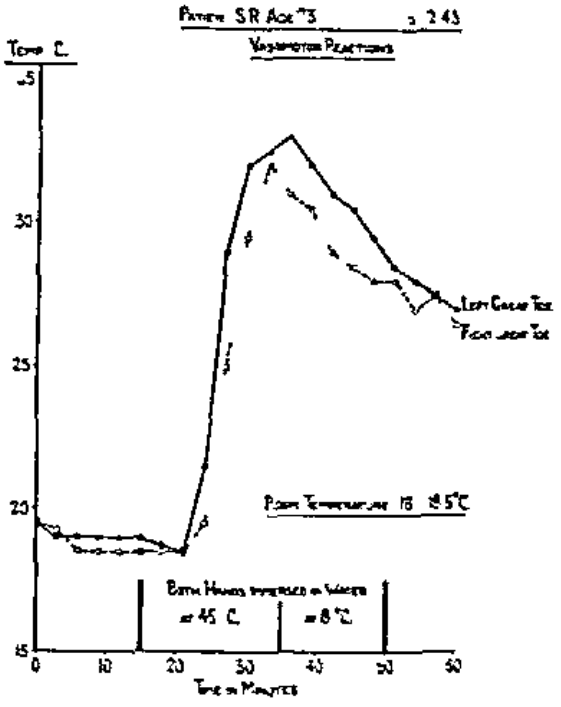

FIG 10
Lower limbs—normal reflex vasodilatation

When one or more limbs are immersed in water as hot as can be conveniently tolerated (44-47°C), vasodilatation will take place in the non immersed limbs after a latent period which varies from 7 to 20 minutes, but is usually of the order of 15 minutes This vasodilatation is most marked in the digits, and once evident it increases very rapidly (Figs 9 and 10) If the warmed indifferent limbs are suddenly cooled by immersion in cold water (5 15 C), vasoconstriction is elicited in the non immersed limbs (Fig. 10)

This is the method which has been used most frequently in the present study The procedure has been as follows The patient, lightly clad, is seated comfortably, and, after a period of acclimatisation, thermocouples are attached to the test digits At least one normal digit is used as a control Readings are made every 3 minutes and with this time interval it has been found practical to make accurate observations on four selected points Room temperature is recorded at least every 10 minutes, either by an additional thermocouple suspended in the air or by an accurate mercury thermometer After a suitable control period,[1] the indifferent limbs (forearms and hands or legs and feet) are immersed in buckets of water (Fig 11) The limbs may be immersed directly in hot water, but in many cases it is better to cool them first by immersion in cold water for about 10 minutes Once a satisfactory degree of vaso-

[1] A period of ten to fifteen minutes is usually adequate for the toes but longer may be required for the fingers

dilatation has been attained, the limbs are removed from the hot water and either allowed to cool by exposure to room air (Fig 9) or immersed in cold water to promote

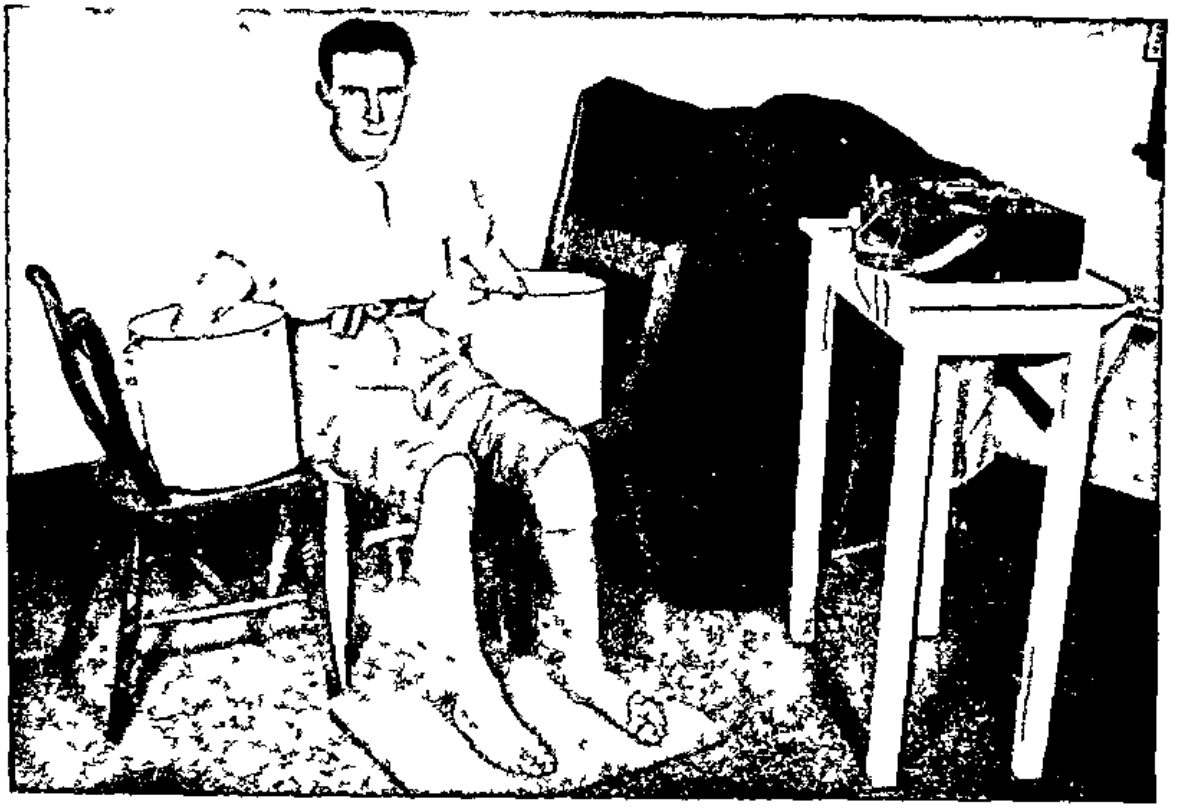

FIG 11
Method of inducing reflex vasodilatation

reflex vasoconstriction (Fig 10) If it is only the capacity of the vessels to dilate that is in question, the latter procedure may be omitted The results are recorded on a graph which, for record purposes, is subsequently photographed and printed

The vasodilator response to the limb immersion method " is dependent upon many of those factors already mentioned in regard to the response to body heating (p 43) In the author s experience vasodilatation in normal hands never fails to occur when the lower limbs are immersed in hot water The reverse is not the case , vasodilatation in the feet may fail to occur when the upper limbs are immersed (Fig 12) This failure of vasodilatation has been recorded by others (Pickering and Hess, 1933 , Uprus *et al* , 1936), and does not necessarily indicate a defect in nervous conduction or any structural change in the blood vessels of the lower extremity With this exception the method is found

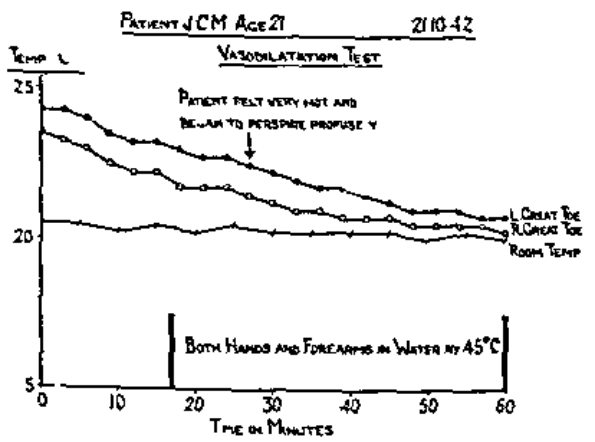

FIG 12
Failure of reflex vasodilatation in normal lower limbs (cf Fig 18)

to be exceedingly reliable It is not unduly discomforting to the patient, and is the most satisfactory method when it is necessary to compare the vascular responses of the upper limbs

The physiology of reflex vasomotor responses is not simple On the afferent side there are two possible routes by which stimuli may reach the central regulating mechanism in the hypothalamus warmed (or cooled) blood returning from the immersed limbs may act upon a thermo sensitive vasomotor centre , alternatively, afferent stimuli originating in thermal or other receptors in the immersed limbs may reach the vasomotor centre along nervous pathways Martin (1930) and Fulton (1943) state that the hypothalamic nuclei responsible for the regulation of body temperature are responsive both to nervous impulses arising from thermal receptors in the skin and to the temperature of the circulating blood There is abundant evidence that reflex vasoconstriction in response to cooling a limb is dependent both upon afferent nervous impulses and upon cooling of the blood Reflex vasoconstriction results from the application of cold to a limb, the circulation in which has previously been arrested by a sphygmomanometer cuff inflated to a pressure greater than the patient's systolic blood pressure[1] (Pickering 1932) When immersed limbs are suddenly removed from hot water and placed in cold, there is an immediate vasoconstriction in the non immersed limbs , this is followed by a slight rise in temperature and then by a further progressive cooling The initial vasoconstriction is the result of a nervous reflex as a simultaneous record of rectal temperature shows that blood temperature is still rising, hence the brief rise in temperature which follows The second progressive fall in temperature is preceded by a fall in blood temperature (Uprus *et al* , 1935) Until recently opinion has been against a nervous afferent pathway for reflex vasodilatation Pickering (1932) and Gibbon and Landis (1932) were unable to obtain reflex vasodilatation by heating occluded limbs Uprus and his colleagues (1935 and 1936) found that a rise in rectal temperature always preceded peripheral vasodilatation Heating an insensitive limb will result in dilatation in non immersed limbs reflex vasodilatation will result from heating the lower limbs in cases of transverse myelitis (Gibbon and Landis,

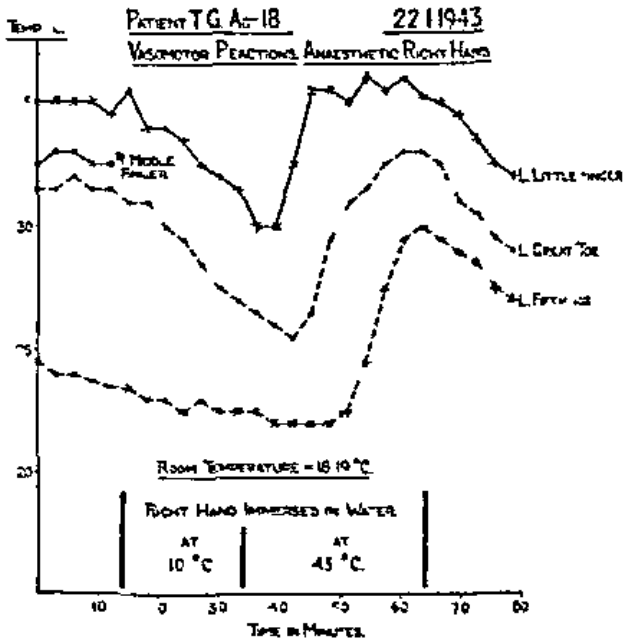

FIG 13

Complete lesion of right brachial plexus—note reflex vasomotor responses in left hand and foot to immersion of the insensitive right hand and wrist

[1] Hereafter referred to as " occluded limbs "

1932, Uprus *et al*, 1935), and from heating an insensitive hand following a complete tear of the brachial plexus (Fig 13) There is always an appreciable delay between the application of heat and the onset of reflex vasodilatation this is in keeping with the hypothesis that the afferent pathway is via the blood stream and not via the nervous system Duthie and Mackay (1940) were able to obtain reflex vasodilatation by heating occluded limbs, provided that the limbs were chilled before immersion in hot water They believe that the failure of previous workers to obtain this response may have been due either to a low environmental temperature which might inhibit reflex vaso dilatation, or to pain which is an early symptom of heating an occluded limb at 45 C, and which may exert a powerful vasoconstrictor influence They believe that the vasodilatation is the result of a nervous reflex, and suggest that the afferent impulses concerned may arise from stimulation of nerve endings in cutaneous blood vessels The hypothesis that reflex vasodilatation is of nervous origin is also supported by Beattie (1938) who suggests that the delay in onset is the result of the deep situation of the Ruffini endings[1] (heat receptors) in the skin Duthie and Mackay (1940), however, were able to obtain a response from heating an occluded therm anaesthetic limb Further evidence that afferent sensory impulses may be responsible for reflex vasodilatation is mentioned by Wilkins (1942) Exposure of the trunk to radiant heat which does not penetrate deeply may cause peripheral vasodilatation although the rectal temperature is falling, conversely, a single blast of cold air may inhibit reflex vasodilatation even if the rectal temperature is rising The pathway along which such afferent nervous impulses might pass has not yet been determined Section of the preganglionic sympathetic fibres to the arm does not result in an interruption of the impulses (Duthie and Mackay, 1940) The crucial experiment of heating an occluded insensitive limb is not without danger On the basis of present knowledge it seems justifiable to assume that both reflex vaso-dilatation and vasoconstriction may depend upon afferent nervous impulses *and* alterations in blood temperature

The efferent pathway is the sympathetic nervous system Lewis and Pickering (1931) showed that vasomotor changes in the extremities in response to warming or cooling the body are effected through sympathetic nerve fibres This is also true of the reflex responses obtained by the "limb immersion method" since they are absent in a sympathectomised limb (Fig 14) The precise nature of the peripheral mechanism responsible for the vasodilatation is not certain Reflex vasodilatation is essentially an acral phenomenon the proximal portions of the limbs are affected very little (Fig 15) Part at least of the rise in temperature in the proximal portions of the limbs is due to warm blood from the hand or foot returning along subcutaneous veins This factor can be eliminated by the application of a sphygmomanometer cuff inflated to a pressure higher than systolic blood pressure around the wrist or ankle Thereafter reflex vasodilatation is elicited in the proximal portions of the limbs only when heating is pushed to an uncomfortable degree (Grant and Holling, 1938) The vessels concerned are those of the skin and subcutaneous tissue Records

[1] According to Woollard *et al* (1939) heat receptors are not the same as Ruffini pressure endings and are disposed more superficially in the skin

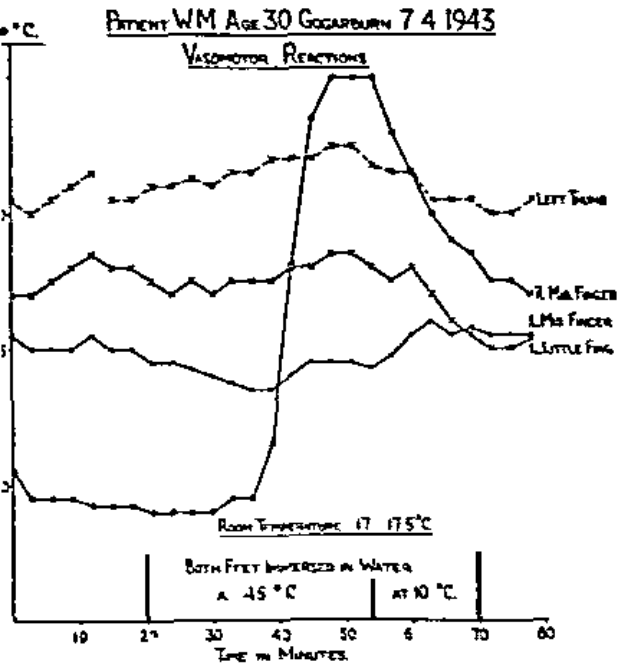

FIG 14

Left preganglionic sympathectomy—note absence of reflex vasomotor responses in digits of left hand

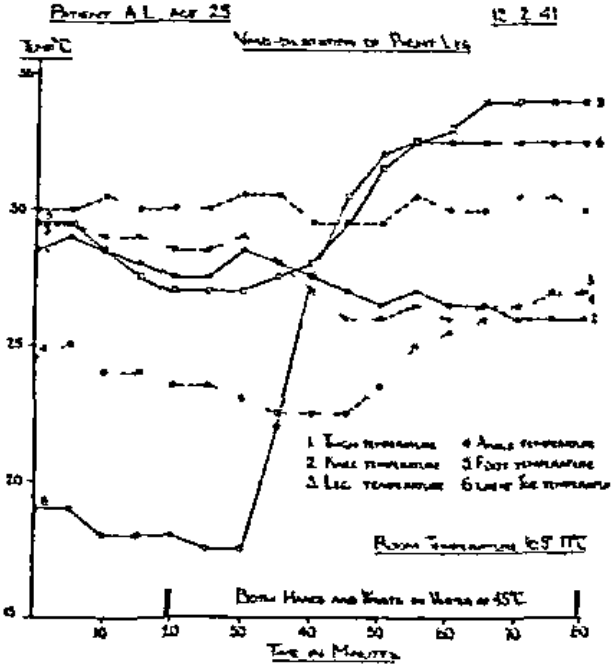

FIG 15

Reflex vasodilatation in normal lower limb, note rise in temperature in acral portions of limb only

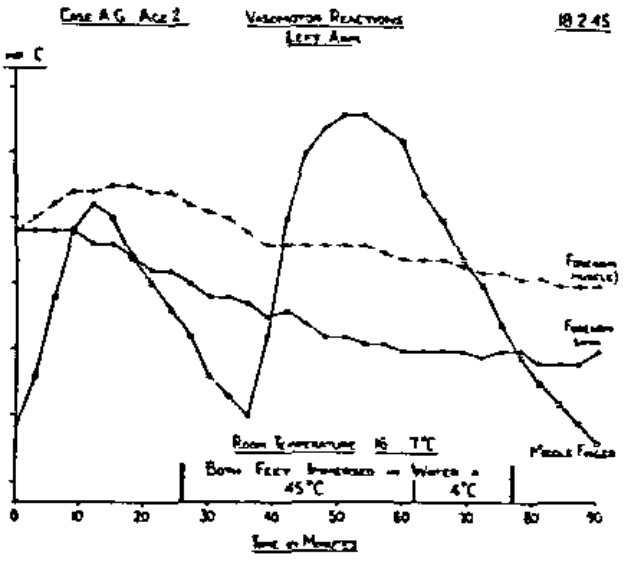

FIG 16

Reflex vasodilatation in normal upper limb note absence of response in skin and muscle of forearm

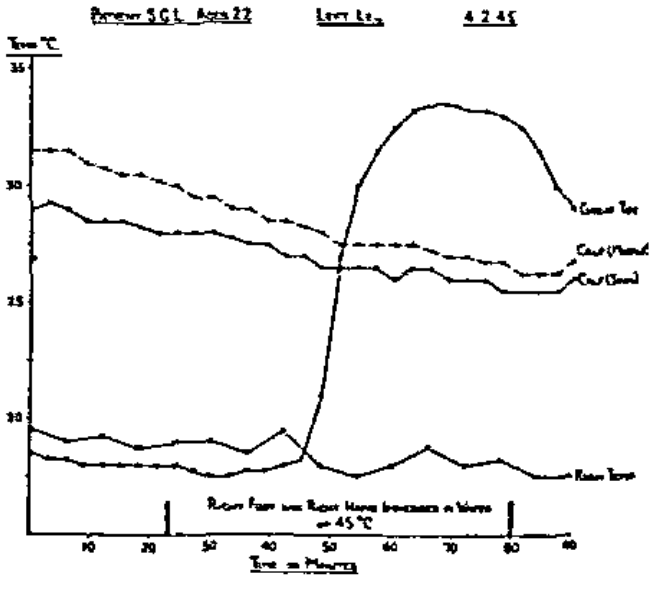

FIG 17

Reflex vasodilatation in normal lower limb, note absence of response in skin and muscle of calf

of muscle temperature have been obtained by inserting a thermocouple in a hollow needle into the muscles of the forearm and calf (Figs 16 and 17) It will be noted that, even when heating is continued for a considerable period, muscle temperature does not rise during reflex vasodilatation [1] It is also significant that a *fall* in muscle temperature does not take place corresponding to the rise in skin temperature It has been suggested that the mechanism of reflex vasodilatation is an increase in blood flow to skin at the expense of that to muscle The evidence of these experiments is against such a view According to Lewis (1927) dilatation of arterioles is most capable of increasing cutaneous blood flow and raising skin temperature Sympathetic vasoconstrictor tone is exerted most strongly upon these vessels when this is released arteriolar dilatation will occur This is probably the important factor in reflex vasodilatation Opening of arteriovenous anastomoses is another factor and with the predominantly peripheral distribution of sympathetic fibres explains the acral nature of the response The minute cutaneous vessels play little part in the response since the extremities do not as a rule become flushed and cutaneous hyperaemia is not necessarily associated with any marked rise in skin temperature (p 54)[2] Evidence which has been presented elsewhere (p 16) suggests that in addition to the inhibition of vasoconstrictor tone, active vasodilatation mediated through sympathetic vasodilator fibres may play a part in the response It seems possible that the response is initiated through vasodilator fibres and that, once vasodilatation has begun, inhibition of vasoconstrictor tone follows

3 DIAGNOSTIC NERVE BLOCK

In 1929 Lewis utilised the procedure of anaesthetising the ulnar nerve at the elbow by the injection of novocaine to study the rise in temperature which followed in the little finger In the following year, White (1930) advocated the blocking of peripheral nerves by procaine as a satisfactory test for determining the vasodilatation which might be expected to follow the operation of sympathectomy Brill and Lawrence (1930), Morton and Scott (1931) and Telford and Stopford (1932), demonstrated that for the lower limbs spinal anaesthesia was equally effective These tests all depend upon the fact that sympathetic vasoconstrictor fibres are amongst those which are most susceptible to the procaine group of drugs and are thus readily blocked *The centrifugal impulses which maintain vasoconstrictor tone are therefore* interrupted and vasodilatation results The vasoconstrictor fibres may be blocked at any point between the spinal cord and the periphery In practice three methods are employed —

(*a*) **Spinal Anaesthesia** —This method is applicable to the lower limbs only The aim is to block the preganglionic sympathetic fibres in the anterior spinal roots The technique is similar to that employed for any spinal anaesthetic except that it is more important to block anterior than posterior roots The anaesthetic is administered with the patient sitting Depending upon whether a heavy or light anaesthetic[3]

[1] In the case of the lower limb similar results have been reported by Friedlander *et al* (1938)

[2] The role of the main arteries of the limb in reflex vasodilatation is discussed later (p 66)

[3] The author uses 3 c c of 5 per cent procaine

is used, he is then allowed to lie on his face or back In this way the anaesthetic will affect both limbs equally and the responses can be compared The level of anaesthesia is important Since the preganglionic supply to the lower limbs extends from tenth thoracic to second lumbar segments inclusive an anaesthesia as high as T10 is required A low spinal anaesthetic may paralyse the feet and make them insensitive without effecting a vasomotor paralysis On the other hand, a spinal anaesthetic which extends much higher than T10 will paralyse the vasomotor fibres to the splanchnic vessels and cause a fall in blood pressure which may prevent or delay the onset of peripheral vasodilatation For this reason, a record of blood pressure should be kept If the anaesthetic is properly administered, vasodilatation will appear in from 10 to 15 minutes, and be complete within 30 minutes (Fig 18) This method has the advantage that nervous vasoconstrictor impulses are known to be abolished and therefore any failure in response must be due to a vascular defect, thus spinal anaesthesia will induce vasodilatation in feet which have failed to respond to reflex vasodilatation (cf Figs 12 and 18) An opinion contrary to this view has been expressed by Wright and Phelps (1940) Using a plethysmographic technique, they studied the blood flow to the leg and foot in response to various procedures which cause peripheral vasodilatation amongst these were spinal anaesthesia and sciatic nerve block They found that spinal anaesthesia to T10 did not increase blood flow and that in each case heating the upper extremities produced an increase in blood flow in the presence of the motor and sensory paralysis due to the spinal anaesthesia' Sciatic nerve block on the other hand caused a marked increase in blood flow and there was no further increase from reflex vasodilatation or from the application of local heat They interpret these findings as indicating that spinal anaesthesia does not cause full vasodilatation and that some vasomotor fibres to the lower limbs (and presumably in the sciatic nerves) remain unaffected by a spinal anaesthetic as high as T10 They do not explain how these fibres reach the lower limb These findings differ from those recorded by other observers Wright and Phelps point out that in their experiments the skin temperature of the feet was high (31 32 C) before the spinal anaesthetic was administered A skin temperature of this level would be regarded by many observers as an indication of normal vasodilatation In normal limbs satisfactory spinal anaesthesia will raise the skin

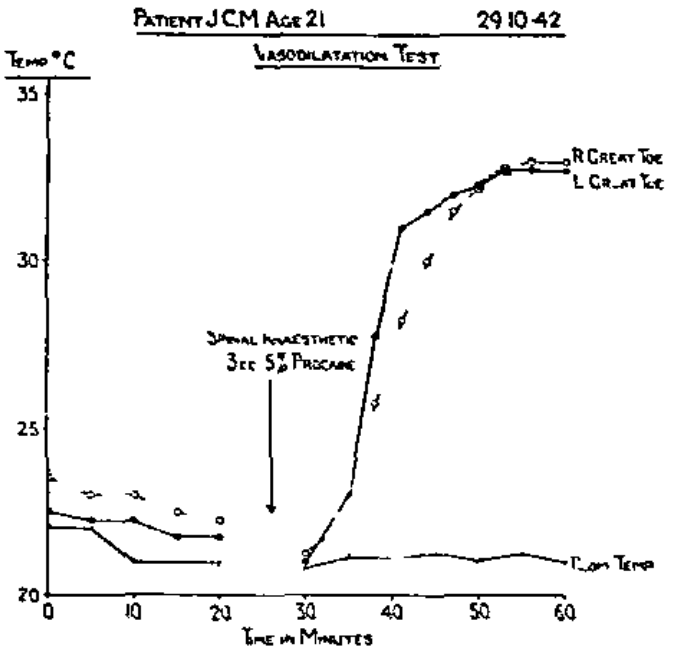

Fig 18
Vasodilatation induced by spinal anaesthesia (same case as Fig 12)

temperature of the toes to 34-35°C, and in the present study this has been regarded as "normal vasodilatation level" for spinal anaesthesia The response to spinal anaesthesia is the vasomotor test of election for any lower extremity with a doubtful circulation The method is subject to those dangers known to be associated with spinal anaesthesia It is therefore not employed routinely but is reserved for those cases which show an unsatisfactory response to reflex vasodilatation

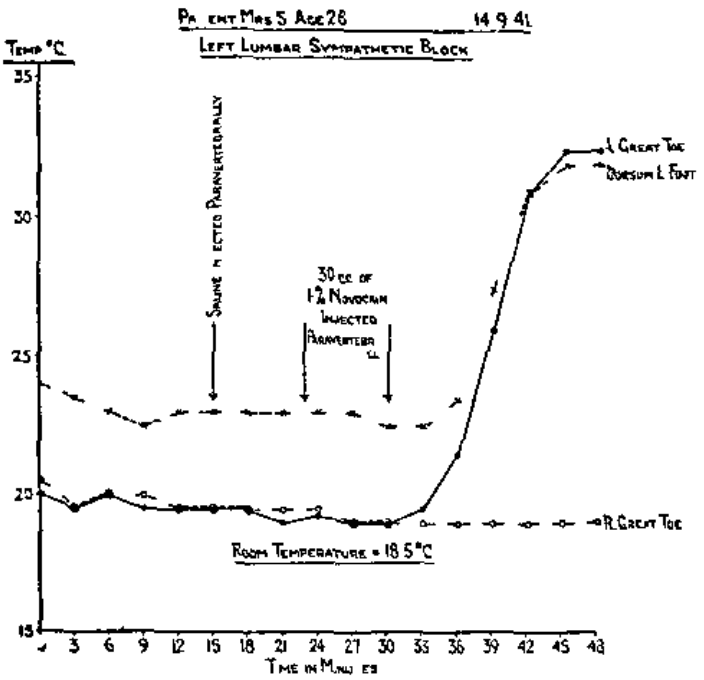

Fig 19
Left paravertebral block—vasodilatation in left foot only

(b) **Paravertebral Injection** — The sympathetic ganglionated chain may be blocked with novocaine either in the upper thoracic region for the upper limb or in the lumbar region for the lower limb The technique of the procedure is now described in most books dealing with the autonomic nervous system or with peripheral vascular disease (for example, White and Smithwick, 1942, *Homans*, 1939) and need not be repeated in detail here It requires a little practice, but once this is acquired the procedure is simple and disturbs the patient very little For the upper limb it is necessary to infiltrate only the second thoracic ganglion, but it is usual to infiltrate the stellate ganglion also so that the presence of Horner's syndrome affords additional confirmation of a successful injection For the lower limb (Fig 19) it is usual to block the second to the fourth lumbar ganglia inclusive This method has been used occasionally in the present study Its chief disadvantage is that unless bilateral injections are

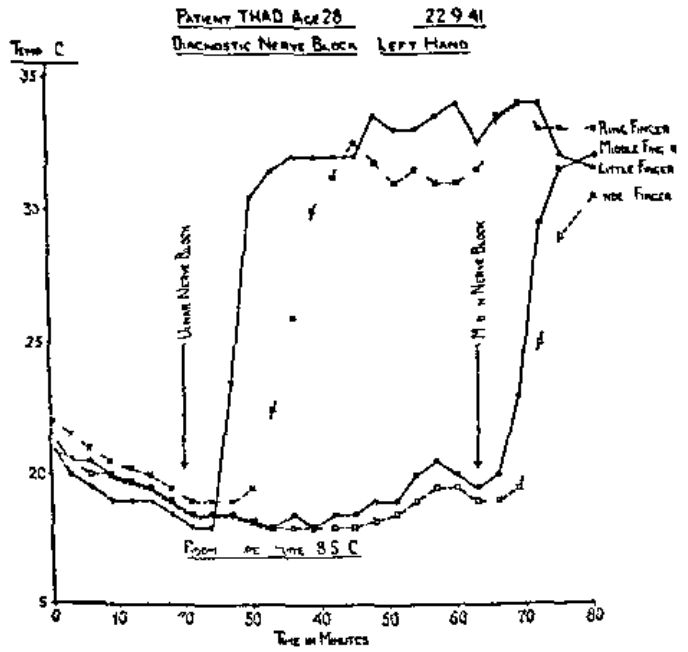

Fig 20
Vasomotor effect of blocking left ulnar and median nerves

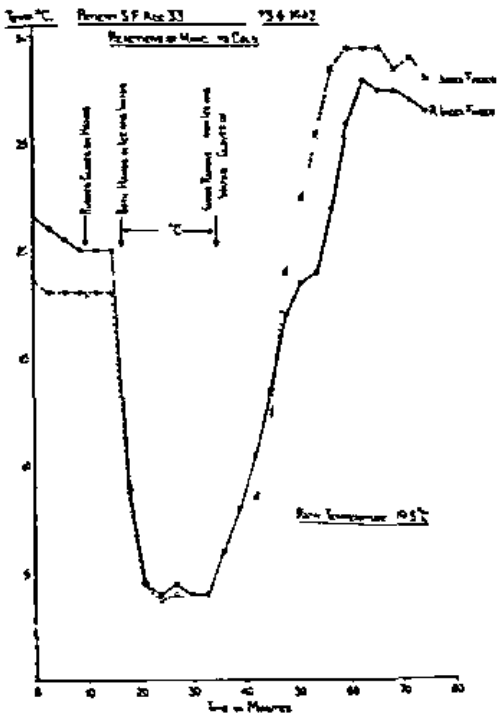

FIG 21
Hands—reaction to local cold—marked vasodilatation

performed, only one limb is affected and the response cannot therefore be compared with that of the other

(c) **Peripheral Nerve Block.**—Certain peripheral nerves viz , in the upper limb, the ulnar behind the medial epicondyle, and the median at the wrist, and in the lower limb, the external popliteal at the neck of the fibula and the posterior tibial behind the medial malleolus, are readily accessible and can be blocked by the injection of local anaesthetic The vasomotor results which follow this procedure are identical with those which appear immediately after nerve division (p 92) At present it is sufficient to state that a vasoconstrictor paralysis results and a rise in temperature is recorded over the territory of the blocked nerve (Fig 20) This test is useful in that it indicates the distribution of the vasoconstrictor fibres of the particular nerve and allows comparisons to be made between individual digits of one extremity. The method has its greatest field of usefulness in the investigation of peripheral nerve injuries where the motor and sensory effects of the nerve block may provide additional valuable information (Highet, 1942)

4 REACTION TO LOCAL COLD

An extremity subjected to the influence of local cold by immersion in ice and water rapidly loses heat and its skin temperature falls If hand or foot be treated in this manner the temperature of the digits falls to within a degree or two of the temperature of the water bath and is maintained at that level (Figs 21 and 22) On withdrawing the extremity from the influence of cold it may show either a characteristic 'warming up'

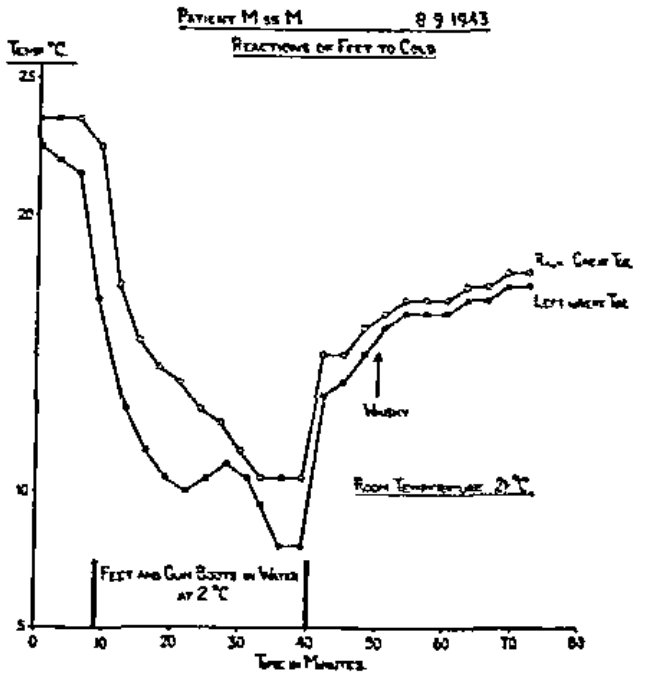

FIG 22
Feet—eaction to local cold—no vasodilatation

reaction (Fig 21) or a very gradual rise of temperature (Fig 22) The former reaction is usually seen in the hand, the latter in the foot Lewis (1930) observed that when a single digit is subjected to local cold it exhibits a characteristic response The temperature of the digit falls initially, but within 5-10 minutes a local vasodilatation is observed The temperature of the immersed digit may be raised 2-3°C, so that a very considerable vasodilatation must take place The vasodilatation continues during immersion, but varies in its intensity so that a phasic rise and fall in temperature is observed If, while the reaction is present, the digit is removed from the cold environment, the temperature will rise above that of neighbouring uncooled digits, be maintained for the next 10-15 minutes, and then subside slowly The reactions of the digits to cold are not observed so well when the whole hand is immersed, but a slight reaction will be noted in Fig 21 These reactions can be obtained on exposure to temperatures as high as 15-18°C, but become more pronounced at lower temperatures Lewis believes that the response is the result of an axonal vasodilatation (p 14) and is thus dependent upon the integrity of the afferent nerve fibres to the digit but independent of the sympathetic nerve supply Grant and Bland (1931) demonstrated that the areas of skin which exhibited these reactions to cold were those supplied with numerous arteriovenous anastomoses, and suggested that opening of these was responsible for the rise in temperature More recently Hertzmann and Roth (1942) have used the photo-electric plethysmograph to study digital vascular reactions to cold They have shown that the immediate cooling of the digit is the result first of a vasoconstrictor reflex, and later the direct constrictor action of cold is superimposed upon this The reactionary dilatation which follows is independent of the vasomotor system, and the vessels taking part are the ' minute pad arteries " The digital arteries do not normally participate in any of the initial reactions to cold, but if the application of cold is continued, they may constrict later

These reactions to cold certainly occur as normal physiological responses and are important in the maintenance of the temperature and nutrition of normal digits Their consideration has been deferred because they are most easily studied by the experimental method of immersion in ice and water, and because the response to local cold has been used as a test of vasomotor activity in certain cases

5. REACTIVE HYPERAEMIA

A period of occlusion of the blood vessels to a limb by means of a sphygmomanometer cuff which is maintained at a pressure higher than systolic blood pressure is followed by one of pronounced cutaneous hyperaemia This reaction, which is known as reactive hyperaemia, has long been familiar to surgeons who use a tourniquet It excited the attention of Lister and was investigated by the German physiologist Bier In the present century it has been extensively studied by Sir Thomas Lewis and his colleagues (Lewis and Grant, 1925, Lewis, 1927) The period of hyperaemia bears a definite relation to the length of the circulatory arrest; provided occlusion is not prolonged for more than a few minutes, the duration of

the hyperaemia is usually a half to three quarters that of the arrest It has been shown that the hyperaemia represents the repayment of a blood flow debt which is built up during the period of arrest in the limb distal to the cuff (Lewis, 1927, Abramson *et al*, 1941) The reaction is dependent upon the accumulation of local metabolites during the period of arrest, and alone of the reactions considered in the present study, it is independent of the nervous system It is thus unaffected by reflex vasodilatation and by the usual vasoconstrictor stimuli, but is dependent upon arterial pressure within the limb (Eichna and Wilkins, 1941) The intense cutaneous hyperaemia is the result of dilatation of the minute vessels and opening of arteriovenous anastomoses, but it is not accompanied by a significant rise in skin temperature (Fig 23), which indicates that larger vessels of the order of arterioles are not involved In using reactive hyperaemia as a test of the circulation to an extremity, the method followed is similar to that described by Pickering (1933) and Lewis (1936) The limbs are first thoroughly warmed to a like temperature by immersion in a water bath at 35 37°C, then elevated and the cuffs applied and inflated During the period of occlusion (usually 3 5 minutes) they are kept warm either by re-immersion in the water bath or by covering them with blankets The pressure is then suddenly released and the flushing of the limbs distal to the cuff observed and timed A normal limb subjected to this procedure will be flushed to the tips of the digits within 10 seconds

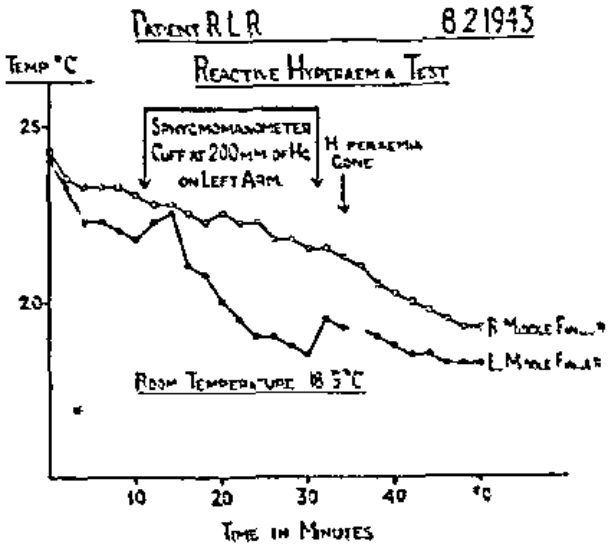

FIG 23
Reactive hyperaemia—only slight rise in temperature with intense cutaneous hyperaemia

SUMMARY

Variations in normal vasomotor activity which are commonly imposed upon the extremities to study the peripheral circulation are described Raising body temperature either by an induced pyrexia or by heating the trunk causes peripheral vasodilatation Reflex vasodilatation induced by the ' limb immersion method " is considered to be a simple and satisfactory method of testing the capacity of the peripheral cutaneous vessels to dilate It is a more reliable test for the upper than the lower extremity a failure of response in the latter need not necessarily indicate any structural disease of the neuro vascular mechanism The physiology of reflex vasodilatation is considered in some detail and it is concluded that the response is the result of both afferent nervous impulses arising in receptors in the immersed

limbs and of a rise in blood temperature The efferent pathway is the sympathetic nervous system, and it is probable that both vasodilator and vasoconstrictor fibres are involved in the production of the vasodilatation The value of diagnostic nerve block (spinal anaesthesia, paravertebral injections and peripheral nerve block) is also considered The vasomotor response to spinal anaesthesia is the most certain method of estimating potential vasodilatation in the lower limbs On exposure to local cold an extremity exhibits a characteristic reaction, and in certain cases this may afford information regarding the peripheral circulation The cutaneous hyperaemia which follows a brief period of circulatory arrest is independent of the nervous system, and is largely the result of dilatation of minute cutaneous vessels

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CHAPTER FIVE

OCCLUSIVE VASCULAR DISEASE

INTRODUCTION

ABNORMALITIES of the circulation to the limbs may result either from disease of the blood vessels or interference with vasomotor regulation The simplest form of defect is that in which as a result of disease there is occlusion, either partial or complete, of the vessels responsible for the inflow of blood to the limb If direct trauma to an artery be excluded, the processes which reduce the amount of blood flowing to a limb may be classified into two large groups (Learmonth, 1938) —(1) An organic change is present from the first in the lumen or wall of the affected vessels (2) the obstruction to blood flow is offered by spasm of the vessels and organic changes are (at least at first) absent

In the present section only cases falling into the first of these large groups will be considered This group may be further subdivided into cases of (*a*) embolism, and (*b*) thrombosis it is with the latter that the studies herein reported are concerned Thrombosis in an artery is most commonly the result of disease of the vessel wall (arteriosclerosis, thrombo angiitis obliterans, syphilis), less commonly it may result from blood diseases (polycythaemia, leukaemia) external pressure (tumour, cervical rib) and as a result of debilitating diseases (pneumonia, typhoid) Leriche and Stricker (1933) described a condition which they called "spontaneous monoarteritis of indeterminate origin" The author has recently seen 4 cases of localised arterial thrombosis occurring in otherwise healthy young adults The clinical picture corresponds to that described by Leriche and Stricker These cases have been reported in detail elsewhere (Learmonth *et al*, 1944), but observations relative to the present study will be considered here

Peripheral vascular disease which is thrombotic in nature is more frequent in the lower than in the upper limbs, and the present observations are confined to the former While thrombosis is the main factor in all the cases considered, it is possible that an element of spasm, either of main vessels or collaterals, may have played a part in the causation of symptoms and the vasomotor disturbances which have been observed This will later be considered in more detail

OBSERVATIONS

(1) **Skin Temperature Gradients** —At the outset of the study it was hoped that observations upon the vasoconstrictor gradient in the limbs after controlled periods of exposure to environmental temperature might provide useful information with

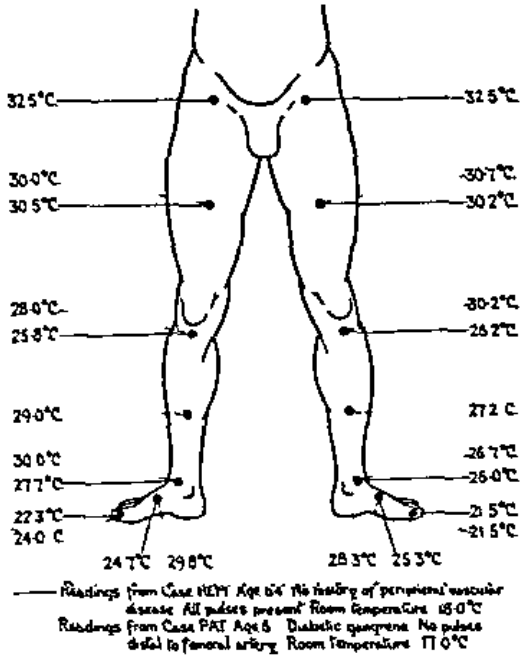

FIG 24

Skin temperature gradients—comparison between limbs of patient with peripheral vascular disease and normal of same age group

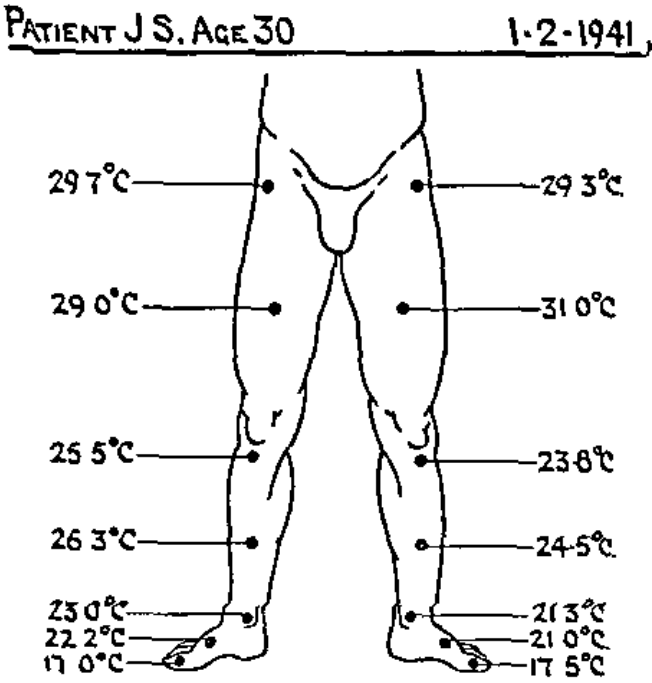

FIG 25

Skin temperature gradients Right leg normal Left leg—no pulses palpable distal to femoral

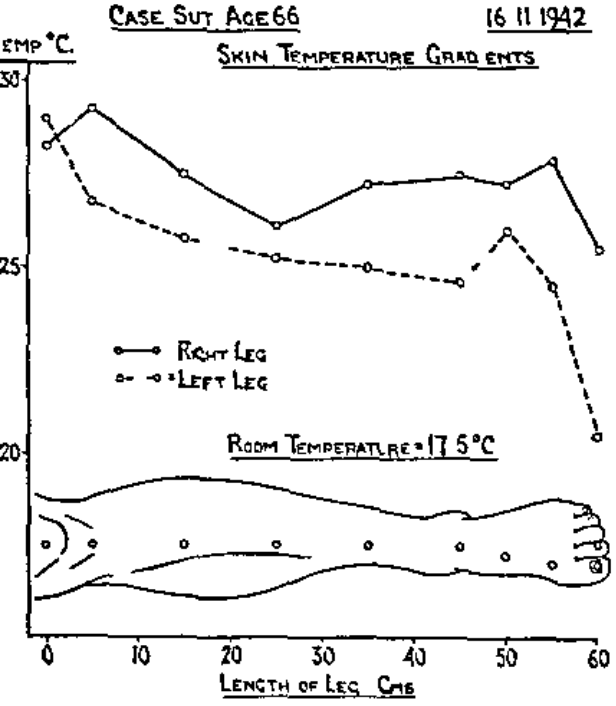

FIG 26

Skin temperature gradients, to show coldness of affected limb

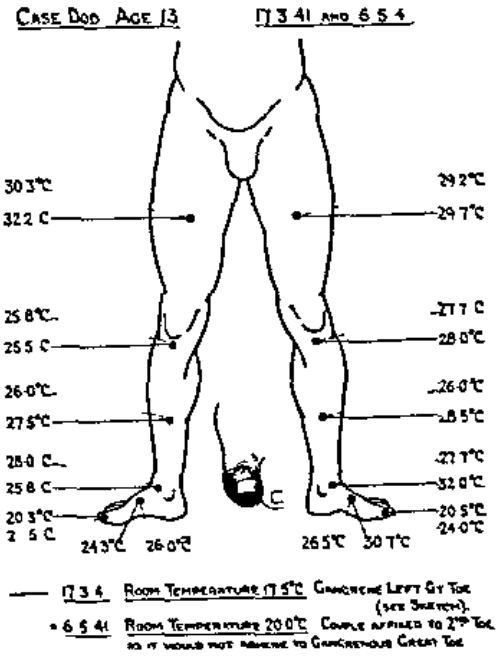

FIG 27

Skin temperature gradients, note high temperature in left foot immediately proximal to gangrenous great toe

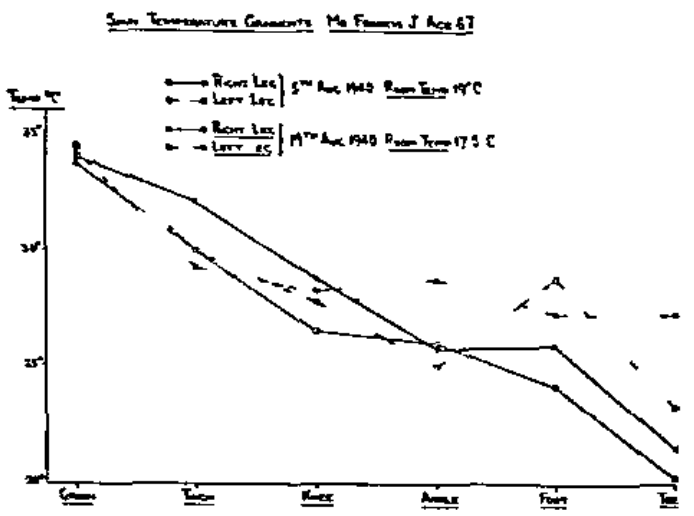

FIG 28

Skin temperature gradients in legs of patient with threatened arteriosclerotic gangrene of left foot showing improvement in skin temperature after two weeks of treatment by reflex vasodilatation

regard to the peripheral circulation in cases of vascular disease This hope has not been realised It was found that a limb which was pulseless and the site of severe claudication pain on exercise might show a gradient which differed very little from that of a normal belonging to the same age group (Fig 24) or from the corresponding normal limb (Fig 25) The common belief that a limb with an impaired circulation is necessarily colder than its fellow is only occasionally true, and depends very largely upon the environmental temperature at the time of the observation From many records it has been possible to find only one (Fig 26) in which there was marked coldness of the affected extremity Occasionally the affected extremity may actually be the warmer and, if superficial gangrene with slight sepsis is present, this, even in the presence of a peripheral circulation known to be precarious, may raise the local skin temperature to a high level (Fig 27) Clinical improvement in the condition of a limb as a result of treatment by rest and reflex vasodilatation (Learmonth 1943) may be accompanied by an appreciable rise in the surface temperature of the extremity (Fig 28)

(2) **Response to Reflex Vasodilatation**—From the foregoing it is apparent that little information of prognostic value is to be gained from observations upon the resting surface temperature of the limbs The ability of the cutaneous vessels to dilate in response to reflex vasodilatation induced by the limb immersion method is more helpful Cases of advanced arteriosclerosis in the elderly or thrombo angiitis obliterans in the young fail to respond even if the disease has not

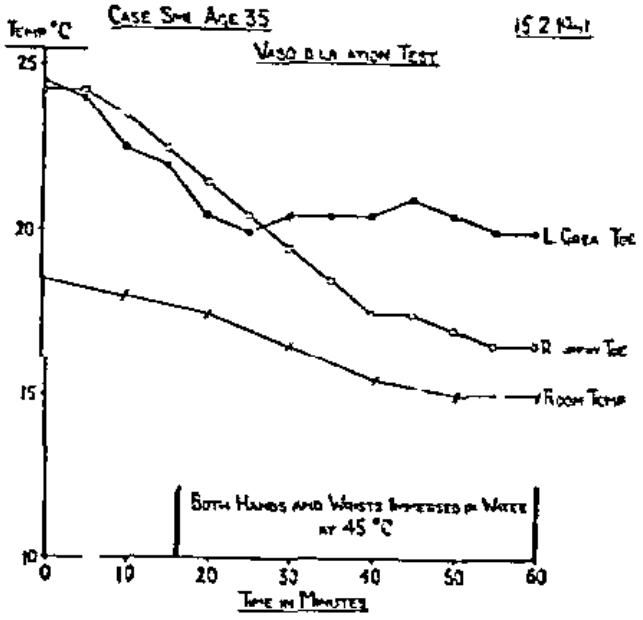

FIG 29

Thrombo-angiitis obliterans—failure of reflex vasodilatation in a case without gangrene or colour changes in the feet

FIG 30

Case 1 Arteriogram showing block in right femoral artery and extent of collateral circulation

blocked at the point where it passes through the adductor magnus muscle The vasomotor responses (Fig 31) showed normal reflex vasodilatation in the left foot , on the right the response was slow and the ultimate level of vasodilatation very poor

Case 2 A ship's plater, aged 42 Five months before admission he sustained a superficial abrasion of the right leg One month later he developed pain in that limb which was characteristic of intermittent claudication This pain persisted and at the time of admission was brought on by walking 100 yards at his normal pace The right foot was colder and whiter in colour than the left The left leg had never caused progressed so far as to cause local peripheral gangrene (Fig 29) Between this complete absence of response and normal rapid reflex vasodilatation, all gradations are to be observed A few illustrative examples may be quoted —

Case 1 [1] An Air Force officer, aged 28, gave a 4 months' history of claudication in the right calf During this time the distance he could walk without experiencing pain became reduced from 2 to 3 miles to 400 yards More recently he had experienced " rest pain " in the limb and a sensation of coldness of the foot On examination, the right popliteal, posterior tibial and dorsalis pedis pulses were absent, those on the left were of good volume Nutritional lesions were not present An arteriogram (Fig 30) demonstrated that the femoral artery was

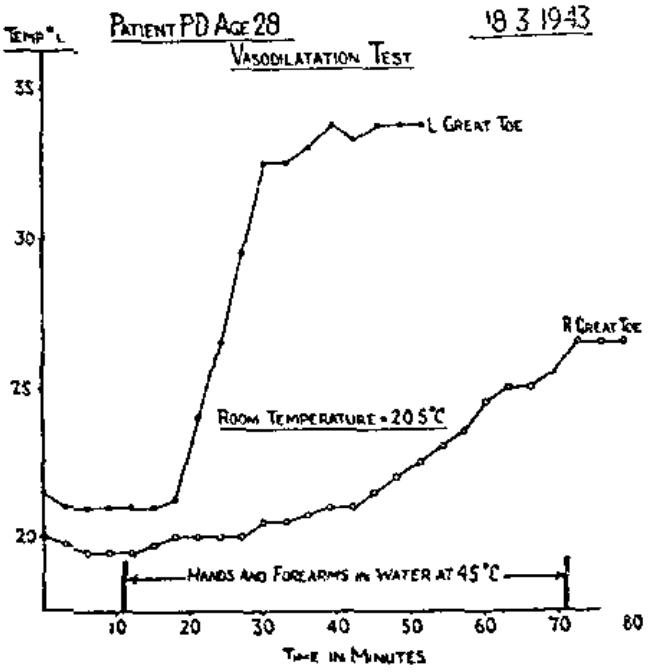

FIG 31

Case 1 Reflex vasodilatation , the response in the right great toe is delayed, gradual and incomplete

[1] Case 3 of Learmonth *et al* (1944)

FIG 32
Case 2 Arteriogram note block in right femoral artery and good collateral circulation

blood pressure was 160 84 mm of Hg and the radial arteries felt thickened and nodular A radiograph of the right hip revealed extensive calcification of the iliac and femoral vessels (Fig 34) and subsequent films showed that this calcification extended throughout the main arterial tree of the lower limbs (Figs 35, 36, 37) The response to a reactive hyperaemia test was moderately good in both feet a flush was present in 15 seconds and maximum in 40 seconds The vasomotor responses (Fig 38), although not normal, were remarkably good for a patient of his years

him any trouble On examination, the posterior tibial and dorsalis pedis pulses were absent on the right, present on the left A reactive hyperaemia test (see p 54) demonstrated that there was a marked difference in the circulation to the limbs The left foot was fully flushed in 30 seconds, the right remained white until 45 seconds after the release of pressure, and thereafter the flush developed slowly and did not attain its maximum intensity until two minutes Arteriography (Fig 32) demonstrated a block in the distal portion of the femoral artery The reflex vasomotor responses in the feet were good and there was little difference between the two limbs (Fig 33)

Case 3 A retired weaver, aged 64, was admitted to hospital with symptoms suggestive of osteo arthritis of the right hip On examination it was noted that the pulsations of the femoral arteries were unduly prominent The

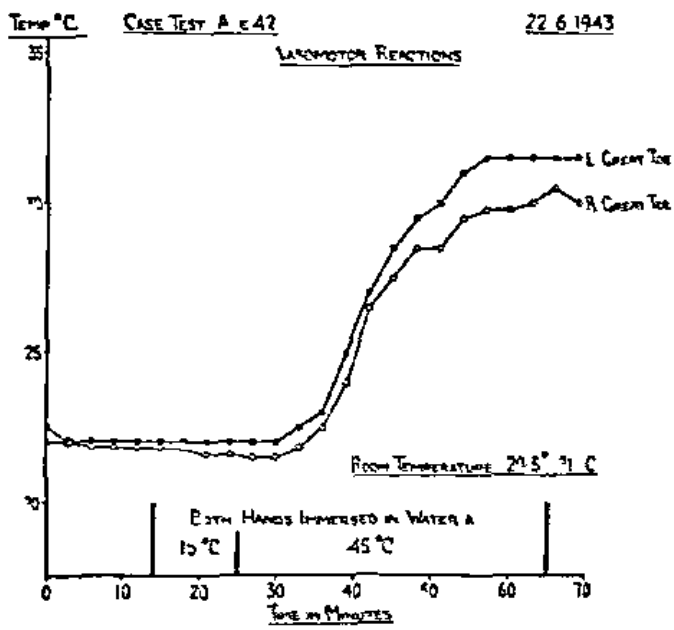

FIG 33
Case 2 Reflex vasodilatation—moderately good response in both great toes

FIG. 34

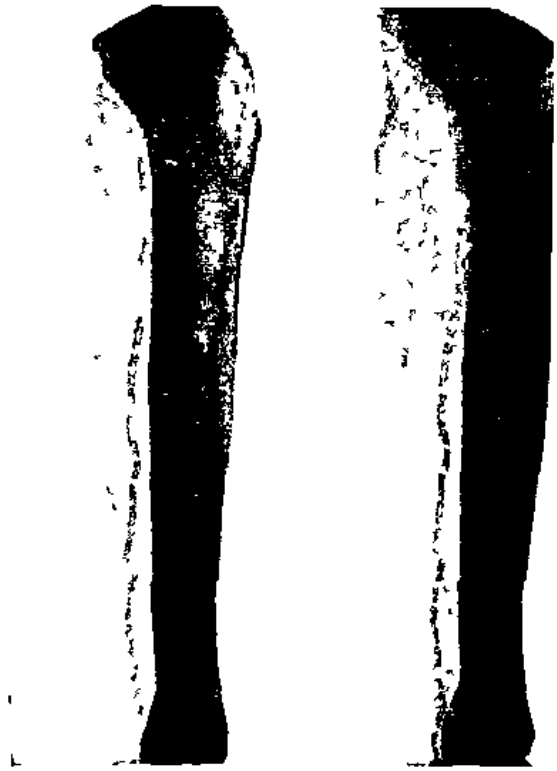

FIG. 36

FIG. 35

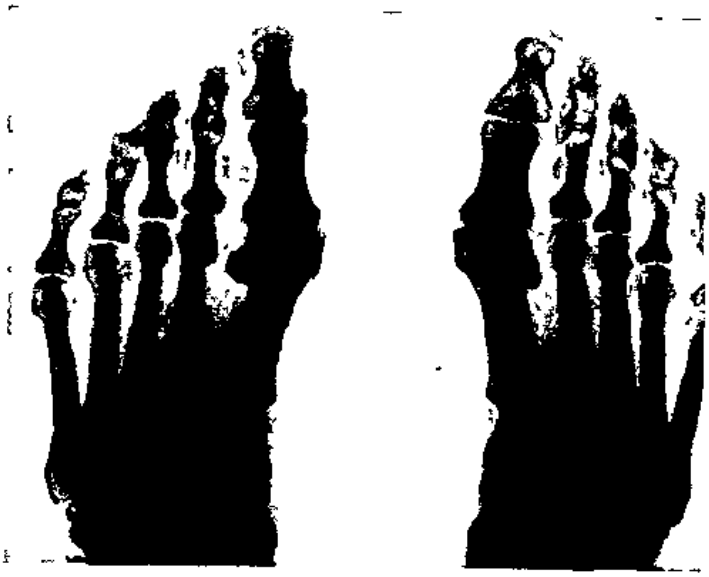

FIG. 37

FIGS 34-37
Case 3. X-rays showing calcification of arterial tree.

Case 4 A soldier, aged 32, was wounded in action, sustaining a compound fracture of the lower end of the right femur Subsequently, there was secondary haemorrhage from the femoral artery, and 2½ years before he came under observation the common femoral artery had been tied in Scarpa's triangle He complained of claudication pain in the right calf on exercise, and of coldness and blueness of the foot On clinical examination the right femoral artery was felt pulsating to a definite level where pulsation ceased abruptly distal to this no pulses could be felt The right forefoot felt colder than the left, but otherwise there was no objective evidence

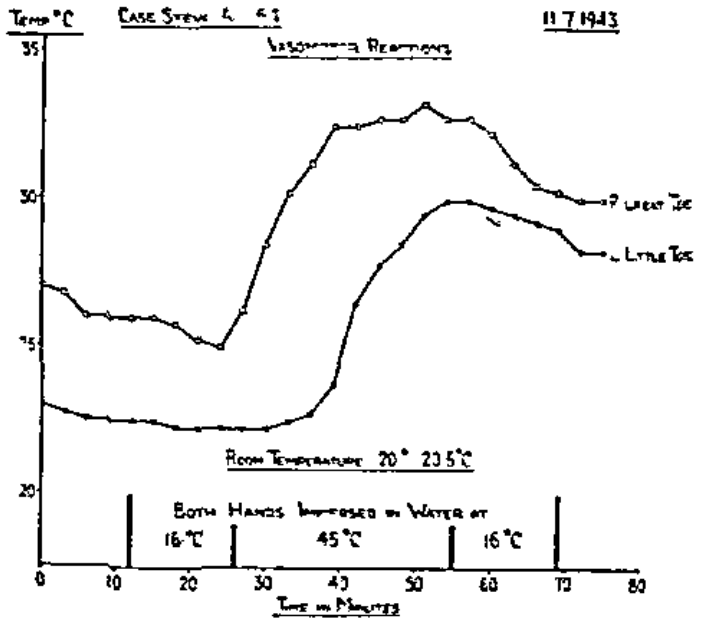

FIG 38

Case 3 Reflex vasodilatation, the response is rather gradual and the ultimate temperature is below normal

FIG 39

Case 4 Arteriogram note filling of right femoral artery distal to block through lateral femoral circumflex vessels

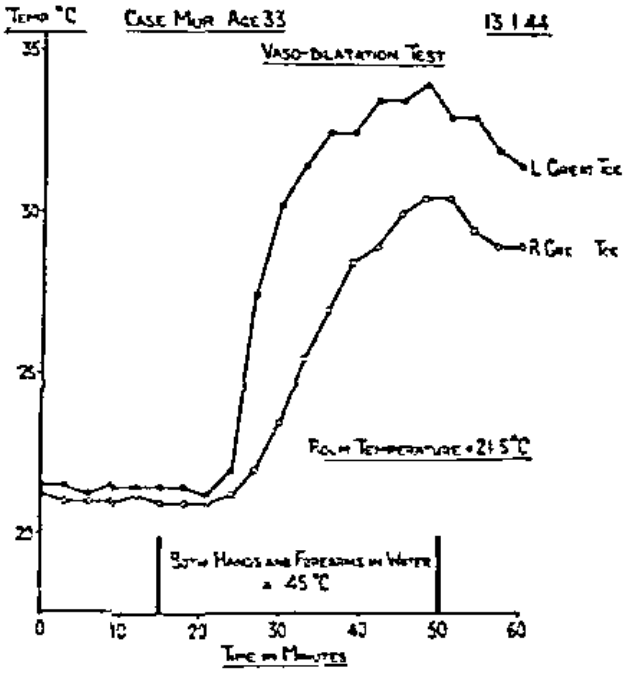

FIG 40

Case 4 Reflex vasodilatation—response in right great toe is good but falls short of normal

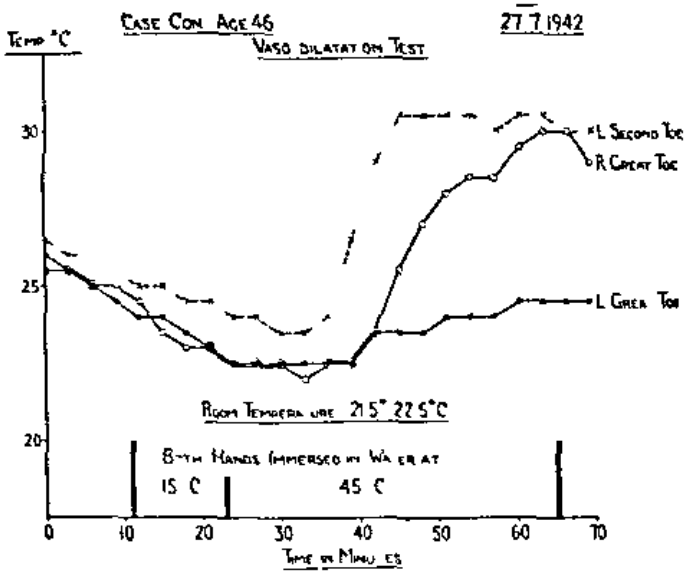

FIG 41

Case 5 Thrombo-angiitis obliterans reflex vasodilatation note the difference in response between the left great and *second toes*

of a diminished circulation The reactive hyperaemia test gave a normal response in the left foot and a poor response in the right (flush appeared in 30 seconds and was maximal in 80 seconds) Arteriography (Fig 39) demonstrated that the right femoral artery was occluded proximally, but distally was patent and well filled through collateral channels Reflex vasodilatation was present in the right foot but diminished compared with that in the normal left foot (Fig 40)

Case 5 A battery sergeant-major, aged 46, gave a history that 8 months previously he had *skinned the left great toe on the* inside of his boot The toe became swollen, very painful, and took many months to heal On examination the dorsalis pedis pulses were both absent, the posterior tibial pulses both present, and a pulse was felt in front of the left lateral malleolus (perforating branch of peroneal artery) The left great toe was deformed, a portion of the terminal phalanx and nail bed being missing The left foot usually felt objectively colder than the *right and was more cyanosed* A reactive hyperaemia test could not be performed as the inflation of the cuffs caused immediate severe pain in the calves Reflex vasomotor responses were present in the toes, but there was a striking difference between the left great and second toes (Fig 41)

(3) **Response to Spinal Anaesthesia.**—Failure to respond to reflex vasodilatation need not necessarily indicate structural disease of the peripheral blood vessels (p 45) Failure to respond taken in conjunction with other evidence such as the absence of peripheral pulses, a history of intermittent claudication,

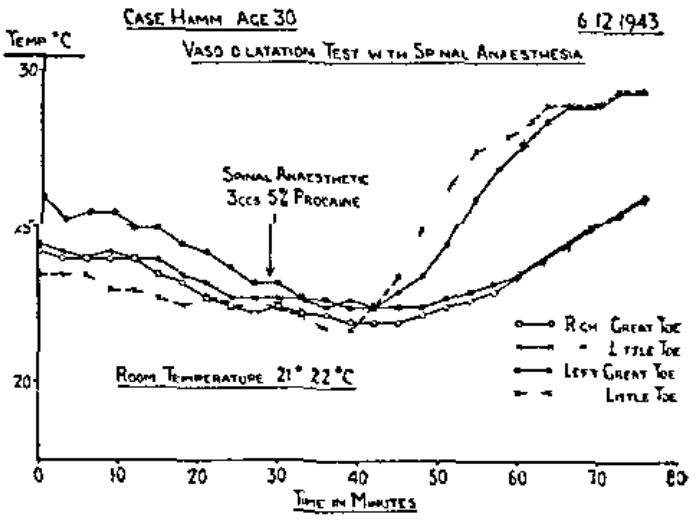

FIG 42

Thrombo-angiitis obliterans—poor vasodilatation in response to spinal anaesthesia indicating a marked degree of occlusion and little or no vasospasm

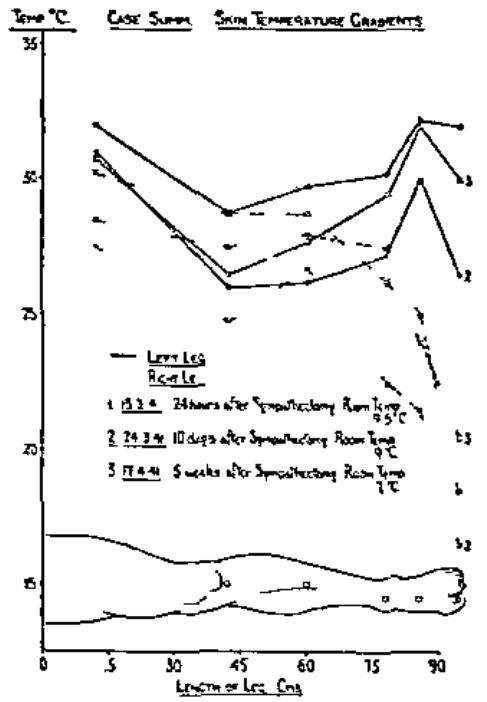

FIG 43
Skin temperature gradients after left lumbar sympathectomy

the presence of nutritional lesions or a poor reactive hyperaemia, is strongly in favour of a diagnosis of occlusive vascular disease There remains a group of cases, usually in young people, in which the history and clinical examination are inconclusive, and the diagnosis depends largely upon a demonstration of the ability of the peripheral vessels to dilate In such cases, if there is any doubt about the response to reflex vasodilatation, spinal anaesthesia should be used, since, by interrupting all nervous vasoconstrictor influences, it demonstrates the maximal amount of vasodilatation possible (Fig 42)

(4) **Effects of Sympathectomy.**—Surgical interruption of the sympathetic nerves to a limb results in a permanent abolition of nervous vasoconstrictor tone As a result, the distal segments of a sympathectomised limb are as warm or warmer than more proximal segments Provided sympathetic denervation is preganglionic and complete, and there is no local vascular factor, then peripheral vaso dilatation will be maintained indefinitely When occlusive vascular disease is present, then the degree of peripheral vasodilatation will depend upon the amount of blood which can reach the surface of the extremity through collateral channels It is generally agreed that a good response to reflex vasodilatation or spinal anaesthesia is an indication for sympathectomy The results of sympathectomy in 2 cases of occlusive vascular disease at intervals varying from 24 hours to 2 years after the operation are demonstrated in Figs 43-45 Figs 43 and 44 are from a case in which the femoral artery

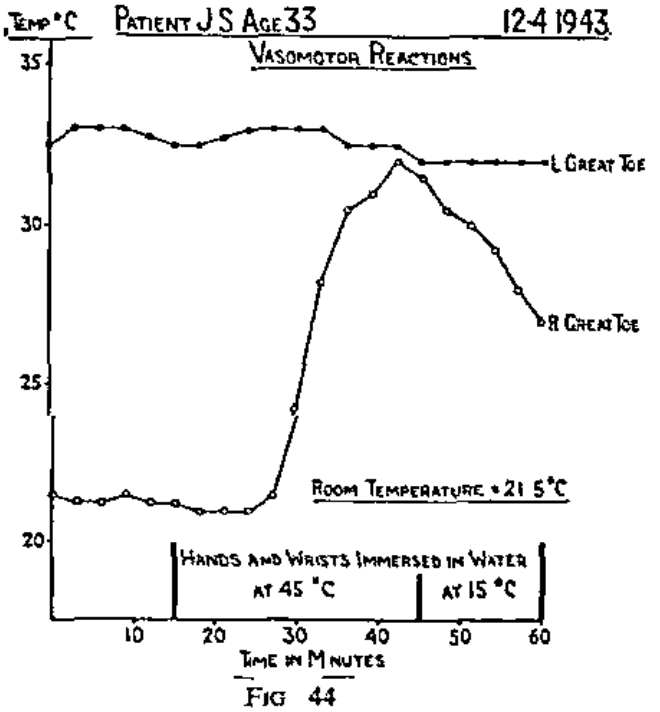

FIG 44
Reflex vasodilatation two years after left lumbar sympathectomy to show maintained vasodilatation in left foot (Same case as Fig 43)

was occluded in the lower third of the thigh (Case 4 of Learmonth *et al*, 1944) Fig 45 is from Case 4 above, where the common femoral artery was ligated in Scarpa's triangle In neither case were peripheral pulses palpable either before or after sympathectomy

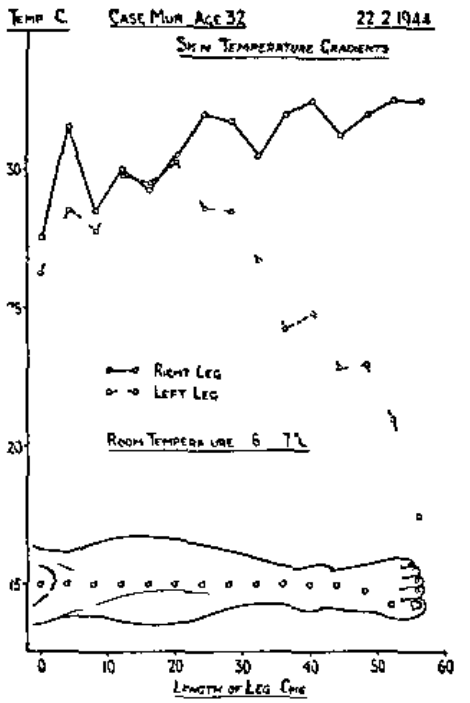

FIG 45

Case 4 Skin temperature gradients 3 weeks after lumbar sympathectomy

DISCUSSION

Cases of peripheral vascular disease present one or both of two groups of symptoms intermittent claudication and peripheral gangrene, either superficial or deep, associated with "rest pain" Intermittent claudication is the result of relative ischaemia of the muscles, while peripheral gangrene is the result of a discrepancy between local tissue demands and the available blood supply Claudication is frequently associated with minor nutritional disturbances in the periphery of the limb, but may occur in a limb which is, to all outward appearances, healthy Young people with thrombo-angiitis obliterans sometimes develop peripheral gangrene without ever having experienced claudication The relative incidence of the two groups of symptoms depends upon the degree to which cutaneous or muscle vessels are affected by the disease process

The nutritional requirements of skin and subcutaneous tissue are slight and fluctuate very little Blood flow to the extremities is normally in excess of their needs (p 39) It follows that a considerable reduction in blood flow to a limb may occur before any peripheral nutritional disturbance becomes apparent According to Kunkel and Stead (1938), the maximal blood flow to the foot (that is, the flow at full vasodilatation) must be reduced to one-third of the normal value before symptoms and "trophic" disturbances develop, but incapacitating intermittent claudication may be present even if the blood flow to the foot is apparently normal

Skin temperature is an index of cutaneous circulation It has already been pointed out that when skin temperature approaches that of the environment, further reduction in blood flow will not be accompanied by a significant drop in skin temperature The reasons for the apparent normality of the vasoconstrictor gradients in limbs affected by occlusive vascular disease thus become evident At environmental temperatures such as prevail in this country, a high degree of vasoconstriction is normally present in the lower limbs (p 33) In cases of occlusive vascular disease the total blood flow to a limb may be greatly reduced without affecting resting skin

temperature It is only when the thermo regulatory function of the extremities is tested that minor defects in cutaneous circulation become apparent If the present observations had been recorded at higher environmental temperatures (24-25°C), it is probable that resting skin temperature gradients would have provided more useful information Any inequality in temperature between two limbs which have been similarly treated is of importance and if local factors such as disuse (*e g* from paralysis) can be excluded the lower temperature is probably due to a reduction in blood supply This reduction may be due to occlusive vascular disease or to a high degree of vasomotor tone, the latter may be normal or abnormal and it is impossible to differentiate these causes by observations upon resting skin temperature The observation that the surface temperature of a limb affected by occlusive vascular disease may be higher than that of the less severely affected corresponding limb has been made previously (Pickering, 1933) and is not so surprising as it appears at first sight If the more vital deep tissues are short of blood as a result of the occlusion of normal channels, nature will attempt to provide them with additional supplies through collateral channels The skin and subcutaneous tissue with its rich network of blood vessels will contribute largely to this, and an increased superficial blood flow will result This hypothesis will also explain the rise in surface temperature which accompanies clinical improvement in a limb as a result of treatment (Fig 28) Freeman (1940) has shown that there is a definite relation between local temperature and the development of gangrene Infection raises local metabolism and increases local temperature (Fig 27) and tissue demands perhaps to a level at which the available blood supply is inadequate and gangrene, or a spread of gangrene, results

In contrast to the superficial tissues, the circulatory requirements of the limb muscles fluctuate considerably Within a matter of minutes an active muscle requires an increase in blood flow amounting to 20 or 30 times resting flow (Grant, 1938) In a limb where the obstruction is in the main vessel and thus reducing total inflow, it is not surprising to find that intermittent claudication is the main symptom and that there is little *clinical* evidence of an impaired cutaneous circulation (Cases 1, 2 and 4) It is, however surprising to find that the cutaneous blood flow at the periphery of the limb can be increased to the extent which is indicated by the rise in skin temperature on reflex vasodilatation (Figs 31, 33 and 40) This raises the problem of the vascular effector mechanism of reflex vasodilatation Is reflex vasodilatation invariably associated with an increase in total blood flow to a limb, or may it be the result of redistribution of blood within the limb? In the hand, Brown and Allen (1941) have recorded increases over resting blood flow as high as 200 per cent, the increase in the forearm being appreciably less In the cases mentioned above, it is difficult to believe that increases in blood flow of this nature could occur, for in three (Cases 1, 2 and 4) the femoral artery is completely occluded, and in a fourth (Case 3) the state of the arterial tree is such as to indicate that any dilatation of large vessels is improbable It appears that reflex vasodilatation in an extremity can occur without the participation of the main blood vessel of the limb It is possible that when body temperature is raised by warming indifferent limbs the needs of a limb become subordinate to those of the body as a whole If more blood cannot

enter the limb, blood might be diverted to the periphery to increase heat loss Such a mechanism appears to be unphysiological, as it would tend to cause muscle ischaemia The alternative is an increase in total inflow to the limb through patent collaterals This appears to be a more likely explanation Limbs showing a good response to reflex vasodilatation after occlusion of a main vessel have had an excellent collateral circulation as demonstrated by arteriography (Figs 32 and 39) In cases with an absent or poor response, either the available collateral circulation is inadequate or reflex vasodilatation fails to induce dilatation of collaterals Leriche has long taught that a thrombosed segment of artery acts as a focus of irritation and is capable of maintaining spasm not only of main arteries but also of collateral channels (Leriche and Stricker, 1933 , Leriche, 1939) If this be true, then it may be impossible to release this spasm by reflex methods Learmonth *et al* (1944) have noted that after preganglionic sympathectomy in a limb with a thrombosed artery the surface temperature of the foot may be higher than was to be expected from the response to reflex vasodilatation they suggest that this observation is in favour of Leriche's hypothesis Spasm imposed upon collaterals through sympathetic pathways may be operative in those cases in which, after failure of reflex vasodilatation, spinal anaesthesia gives a relatively good response

Patency of the small peripheral arteries is essential before reflex vasodilatation can occur The difference between two adjacent digits (left great and second toes Fig 41) makes this quite evident Similar differences between adjacent digits have been observed in the upper limb (Case 1 of Learmonth *et al* , 1944)

From these and other observations the author is of the opinion that the patency of cutaneous arteries and arterioles is the important vascular factor [1] in determining the presence or absence of reflex vasodilatation within a limb Provided that the potential total inflow of blood to the limb is sufficient to allow for even a slight circulatory reserve, some rise in temperature, either in response to reflex vasodilatation or to spinal anaesthesia, ought to be obtainable

The results of sympathectomy ought to afford additional evidence in support of this hypothesis The results recorded above (Figs 43-45) and in a case reported elsewhere (Richards and Learmonth, 1942) indicate that even in the presence of occlusion of a main artery sympathectomy is capable of maintaining an increased cutaneous blood flow If this is the result of a redistribution of available blood within the limb, then following sympathectomy muscle blood flow ought to be reduced The immediate effect of division of peripheral nerves is similar to that of sympathectomy Cohen (1944) has suggested that in a limb after injury to both main vessels and peripheral nerves, the development of Volkmann's ischaemia may be favoured by the pooling of available blood in cutaneous vessels Until recently, opinion was unanimous that sympathectomy did not benefit intermittent claudication Freeman and Montgomery (1942) and Ives (1943) have published results which show that in certain cases clinical improvement in claudication may follow sympathectomy A physiological basis for this observation has been provided by

[1] Throughout this discussion it is assumed that nervous conduction is normal and that the only defect is on the vascular side

Barcroft *et al* (1943) who have demonstrated that there are sympathetic vasoconstrictor fibres to the vessels of human skeletal muscle In man, sympathetic stimulation or adrenalin release causes an increase in muscle blood flow (Grant and Pearson, 1938 Kunkel *et al*, 1939), an observation which appears to be at variance with the clinical results of sympathectomy It is probable that sympathetic stimulation constricts arteries and arterioles but dilates the large muscle capillary bed, sympathectomy releases the vasoconstrictor tone of the arteries and arterioles and thus increases muscle blood flow (Freeman and Montgomery, 1942) Since not all cases are benefited, it is probable that the circulatory reserve of the affected limb is the all important factor If the potential pre operative blood flow of the limbs is barely adequate for nutritional needs, then sympathectomy may divert blood from muscles to skin and thus favour the development of muscle ischaemia The clinical evidence is against such an hypothesis in the author s experience sympathectomy does not make intermittent claudication worse If there is a certain amount of circulatory reserve or if vasospasm is a contributory factor, then sympathectomy ought to increase total blood flow to the limb and thus improve both cutaneous and muscle circulation

In animals it is known that sympathectomy causes a permanent increase in the blood flow through the femoral artery (Herrick *et al*, 1932, Baldes *et al*, 1941) and increases collateral circulation after ligation of a main vessel (Theis 1933) In man the problem remains unsolved and suggests the need for controlled observations on the development of intermittent claudication before and after sympathectomy

SUMMARY

Observations upon the circulation to the lower limbs in cases of occlusive vascular disease are presented It is found that skin temperature gradients made upon resting limbs are of little prognostic value The reasons for this are discussed The response to reflex vasodilatation, or, if that fails, to spinal anaesthesia, is of considerable value in determining the potential inflow of blood to a limb Reflex vasodilatation may occur in a limb even in the presence of occlusion of a main artery It is considered that in this case the degree of reflex vasodilatation represents an increase in total inflow of blood to the limb through collateral channels Patency of cutaneous arteries and arterioles is essential for the occurrence of reflex vasodilatation in a given area (for example a digit) The effects of sympathectomy in occlusive vascular disease are considered It is believed that sympathectomy causes an increase in total blood flow to a limb, and not pooling of blood in cutaneous vessels at the expense of the deeper and more vital tissues

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CHAPTER SIX

THE RAYNAUD PHENOMENON

INTRODUCTION

IN 1862 Maurice Raynaud published his thesis entitled "On Local Asphyxia and Symmetrical Gangrene of the Extremities," and from that day until the present the term "Raynaud's Disease" has been loosely applied to a wide variety of clinical conditions which are associated with those features of asphyxia and symmetrical gangrene which Raynaud described so fully. This is misleading, but much of the misunderstanding with regard to the use of the term has arisen because in his thesis and subsequent publication (1874) Raynaud described not a new disease, as he believed, but a series of local conditions which might occur in the extremities as incidents during the course of many forms of peripheral vascular disease In Raynaud's original series of 25 cases one may detect at least 10 different diseases What Raynaud undoubtedly did do was to give an accurate clinical description of the phenomena of local digital syncope and local digital asphyxia, and it is fitting that these conditions should now be known as the Raynaud phenomenon In the closing decades of last century the occurrence of the Raynaud phenomenon as a feature of many diseases was stressed by Hutchinson (1886-7) Unfortunately, his teaching appears to have been forgotten, and in later writings (Monro, 1899 , Osler, 1903 Barlow, 1911) one finds the same confusion as exists in Raynaud's original description Within recent years, the researches of Sir Thomas Lewis and his colleagues in this country (Lewis, 1929 and 1936 , Lewis and Pickering, 1934), and Allen and Brown (1932a, b, c) in America, have provided a clearer conception of the problem and have offered an accurate definition of the terms "Raynaud's Disease" and "Raynaud Phenomenon" An excellent survey of the present position is to be found in Hunt's (1936a) critical review

DEFINITIONS

The Raynaud Phenomenon is defined by Lewis and Pickering (1934) as "the active and intermittent closure of small arteries of the order of digital arteries supplying the extremities it shows itself clinically by discoloration of the parts affected they become fully cyanotic or waxy white in colour, often numb, and their temperature falls to that of the surrounding air" This definition is an exact physiological one, and for clinical purposes Hunt's definition is possibly better ' Intermittent pallor or cyanosis of the extremities precipitated by exposure to cold, without clinical evidence of blockage of the large peripheral vessels and with nutritional lesions, if present at all, limited to the skin" (Hunt, 1936a)

Raynaud s Disease—Lewis (1936) defines Raynaud's disease as a condition of intermittent spasm of the digital arteries, and divides cases into two groups, depending

upon the presence or absence of local nutritional changes Allen and Brown (1932a and 1932b) lay down a series of six criteria which must be satisfied before a diagnosis of Raynaud's disease is established —

(1) Intermittent attacks of discoloration in the acral parts
(2) Symmetrical or bilateral involvement
(3) Absence of clinical evidence of occlusive lesions of the peripheral arteries
(4) Gangrene or trophic changes, when present, limited in a large degree to the skin
(5) Two years as a minimal period of duration
(6) Absence of any organic disease to which the vasomotor changes might be secondary

In the present study these criteria have been accepted It is a disease affecting females much more frequently than males According to Hunt (1936a), 99 per cent of cases occur in females, and Allen and Brown (1932c) in a series of 150 cases could find only 7 males whose records satisfied their criteria White and Smithwick (1942) adopt a much wider definition, and quote Dickens's Uriah Heep as a good example of the disease Raynaud s disease is a rare condition , Hunt (1936a) and Johnson (1941) have expressed doubts as to its existence as a clinical entity The Raynaud phenomenon, on the other hand, is a relatively common symptom of many diseases

MATERIAL

The material upon which the present study is based consists of 30 cases exhibiting the Raynaud phenomenon observed between December 1941 and February 1944 Only cases in which attacks were observed personally, or in which the history given by the patient was so typical as to leave no shadow of doubt that attacks had occurred, have been included The cases have been grouped as follows —

CASES EXHIBITING THE RAYNAUD PHENOMENON

Group	Nature	No of Cases
A	Hereditary Cold Fingers	1
B	Raynaud's Disease (1) Females	9
	(2) Males	8
C	Thrombo angiitis obliterans	3
	Arteriosclerosis	2
	Syphilis	2
D	Cervical Rib	1
E	" Pneumatic Hammer Disease "	1
	Exposure to Severe Cold	1
	Fractured Clavicle	1
	Whitlow	1
	Total	30

Males=19 Females=11

A **Hereditary Cold Fingers**—The one case in this group, a male aged 20, gave a definite history of a similar condition in other members of the family, and had experienced cold blue hands all his life with typical attacks of the Raynaud phenomenon commencing about the age of 14 Many of the cases in Group B gave a history of attacks since early youth, but none gave a family history of the condition and are therefore not included in Group A

B **Raynaud s Disease (Females)**—The average age of the patients at the time they came under observation was 41 years, and nearly all gave a long history of typical attacks usually commencing in the late teens Only 2 cases had a history of less than 5 years In 5 of the cases, nutritional lesions, chiefly recurrent whitlows, were the reason for the patient seeking medical advice

Raynaud's Disease (Males)—The 8 cases comprising this group were all members of H M forces The average age was 26 years All were in good general health and showed no abnormality of the cardiovascular system Practically all gave a history of persistent cold blue hands for many years, with a more recent history of typical Raynaud attacks superimposed upon this background The precipitating factors initiating the first attack of the Raynaud phenomenon in some of the cases in this group are of interest and a few examples may be quoted —

(1) *Case LF* This patient, aged 25, was a cinema operator to trade and accustomed to work in a warm environment After joining the service, he was sent to the North of Scotland, and there, while working on a high pylon on a summer day, he experienced "cold fingers" for the first time in his life During the following winter he had several subsequent attacks

(2) *Case RC* A soldier, aged 21, in civil life an oiler of railway locomotives on the Southern Railway, had experienced cold blue hands all his life, but had never suffered from dead fingers After the outbreak of war, he served for a period in a cold dry climate (Iceland) without accentuation of his symptoms, but on being transferred to a cold wet climate (Orkney) in the winter of 1942-43, he had his first typical attack of the Raynaud phenomenon

(3) *Case JM* A youth aged 20 had noted that his hands tended to be rather cold and blue for several years, but had thought very little about it On joining the army he was sent to the North of Scotland During his first week there, he noted that when he arose in the morning and went out of doors, the distal two phalanges of all fingers in both hands became white and numb, and remained like that for 1-2 hours unless he took active steps to warm them

These cases suggest that the rigours of war time service in the field may be operative in changing what is essentially a benign condition into one which may be seriously disabling to the patient

C **Occlusive Vascular Disease.**—The Raynaud phenomenon may appear as a symptom of many forms of peripheral vascular disease It is not a common symptom of thrombo angiitis obliterans In 27 cases of this disease seen during the period under review, typical attacks in the fingers were observed in only 2 cases, and one of these had a cervical rib which may have been an additional causative factor A third case gave a typical history of attacks The 2 arteriosclerotic cases were a man

and a woman, aged 63 and 67 respectively The former gave a history that his father had had similar trouble with his fingers, but as the patient's attacks did not commence until he was over 50 years of age, it seems more likely that the disease rather than the hereditary element was the important factor One of the syphilitic cases commenced with typical Raynaud attacks and subsequently developed bilateral gangrene of the digits It is doubtful if the other case is attributable to syphilis The patient was in hospital receiving a course of anti-luetic therapy when he suddenly experienced a very typical attack He had not had a previous infection, and his Wassermann reaction was negative, but the case is included in this group for want of a better classification

D **Cervical Rib.**—Contrary to general opinion, the Raynaud phenomenon is not a frequent manifestation of the presence of a cervical rib Persistent blueness and coldness of the hand on the affected side is a more common symptom Leriche (1939) has drawn attention to the fact that it is the large cervical rib which most commonly causes vascular symptoms , rudimentary ribs are more likely to cause neurological signs The single case in this group was a woman, aged 38, who experienced her first typical attack during a summer month in the South of England

E **Miscellaneous.**—This group is in many ways the most interesting and the cases will be considered more fully

(1) The Raynaud phenomenon occurring in those who work with vibrating tools is a recognised clinical entity Hardgrove and Barker (1933) described the condition in those who work with pneumatic stone-cutting tools, and called it " Pneumatic Hammer Disease " Legge (1934) has described a similar condition in those who clean brass castings, and Hunt (1936b) observed it in riveters The present case (JL , aged 35, Fig 49), like that described by Lewis and Pickering (1934), occurred in a patient who had worked in a shoe-making factory His work was to hold shoes against a drum which was continually vibrating, and to manipulate levers also attached to the vibrating drum He was 14 years at the trade before symptoms developed, first in the right hand and then in the left By the time he came under observation 10 years later, all fingers of both hands were severely affected, the index fingers most severely He stated that the condition was a known occupational hazard in the trade, and that 8 out of his 10 mates were similarly affected

(2) *Case AM* (Fig 50) An airman, aged 19, " went up " without gloves At 12,000 feet he began to suffer a " fierce ache " in his hands and wrists, but his fingers did not change colour He had to be helped from the plane on landing because his pain was so severe By that evening he had completely recovered After this episode, although suitably clad, he had similar attacks when above 12,000 feet, and on the occasion of his third attack noted that his fingers became discoloured By the time he came under observation 4 years later, he was having frequent attacks at ground level, although he had not been flying for 3 years

(3) *Case SF* In 1936 this patient, a man aged 32, had sustained a bad fracture of the left clavicle In July, 1937, he noted his left hand becoming blue and numb when exposed to cold On joining the army in March, 1942, he was posted to Scotland and there had his first typical attack of the Raynaud phenomenon

(4) *Case JC* This patient, a sergeant aged 42, injured his right index finger with a piece of wire in March 1943 The finger became septic and he lost the nail While the new nail was growing, a process that occupied 4 months, he noted that the tip of the index finger would become blue if exposed to cold By September the whole digit was affected and would become quite blue or occasionally white on exposure to cold The condition spread to involve first the thumb, then the radial side and eventually the whole of the middle finger of the right hand By the date of his admission to hospital (24/1/44), the tip of the ring finger was also affected Throughout the little finger was never involved

Some of the cases in this series have been described previously by Learmonth (1943) The list should not be considered as representative of the occurrence of the Raynaud phenomenon in general It is misleading in many respects The male female ratio, for example, is most unusual for a series of cases of this type, but is the result of the circumstances under which cases came under the author's care A striking feature is the absence of any case exhibiting scleroderma or sclerodactyly, conditions which are frequently associated with the Raynaud phenomenon (Lewis and Landis, 1931 Hunt, 1936a) Hyperhidrosis was not a common complaint in the present series of cases, although one or two of the males in Group B tended to have rather moist palms

CLINICAL OBSERVATIONS

(1) **During Attacks**—Attacks of the Raynaud phenomenon may occur in the digits of either the hands or the feet Because of the greater length of the digital arteries of the fingers, the fact that the hands are more exposed than the feet and are required for fine movements, it is almost invariable for patients to complain of attacks in the fingers only, and the present observations are confined to these The thumb even in severe cases frequently escapes, but in some cases may be affected (for example, in Case JC above) Many observations, clinical and thermometric, have been made during the induction the phase of spasm, and recovery from attacks of the Raynaud phenomenon

Cold is undoubtedly the main factor concerned in the provocation of attacks Cold applied locally to the affected digit, even if the rest of the body is warm, will induce an attack, but if the affected hand be kept warm and the rest of the body cooled, an attack will not be induced The combined effect of local and general cold is a most potent factor and will even induce an attack in apparently normal digits Hunt (1936a) was able to induce an attack by immersion of the whole body in a bath at 12 C for 1½ hours The author has suffered from only one attack of the Raynaud phenomenon, and that occurred on a cold spring day at a height of 3,700 feet on a Scottish mountain He was injudicious enough to remove the glove from his right hand at a time when he was feeling exceedingly cold, and the digital arteries of all the fingers went into spasm In attempting to induce an attack by exposure of a hand to cold (for example, by immersion in cold water), it is noted that there is for each case a critical temperature level at which the digital arteries go into

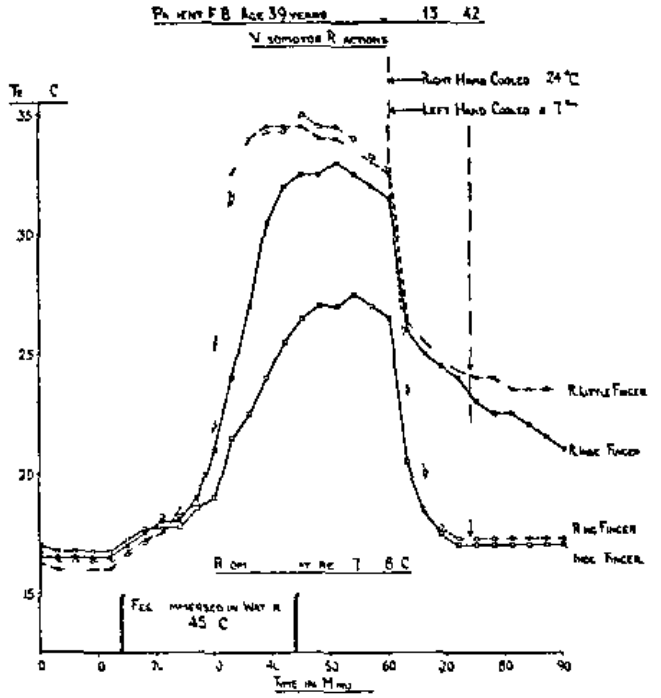

FIG 46

Reflex vasodilatation and induction of attack of the Raynaud phenomenon in the left hand

spasm In the case illustrated in Fig 46, immersion of the warm right hand in water at 24°C failed to induce an attack, but exposure of the left hand at 17°C for a similar period was effective A common mistake is to overcool the digits As Lewis (1929) has shown, cooling to temperatures below 10°C usually fails to induce an attack, because at such temperatures the minute cutaneous vessels dilate, the dissociation of oxy-haemoglobin ceases, and there is a conspicuous after reaction (p 53) with dilata tion of the arterioles and opening of arteriovenous anastomoses, so that the characteristic colour changes of an attack are not observed Cooling the proximal phalanx of a digit is sufficient to cause the whole digital artery to go into spasm Cooling one digit will produce an attack in that digit alone

Emotion may on occasion precipitate an attack, but in the author's experience will do so only if conditions are otherwise favourable when the patient is in a cool room or out of doors, it may cause an attack, but will not do so in a warm room Livingston (1935) describes two cases in which emotional factors were responsible for precipitating attacks of the Raynaud phenomenon in a warm room

An attack usually commences at the tip of an affected digit The tip of the finger becomes pale and this pallor spreads either gradually or rapidly to involve the whole digit (local syncope) Many patients when giving their history state that the digits do not become pale but are always blue or black in colour If the attack lasts, the digits may become a waxy-yellow colour which is most characteristic The deeply cyanosed blue or black colour (local asphyxia) which most patients describe, is due to opening of the minute cutaneous vessels which are then filled by deoxygen ated blood seeping back from the veins Both deep cyanosis and waxy pallor indicate complete arrest of the digital circulation (Lewis, 1936) Pallor of an affected digit is more common if the hand is in use , in attacks observed with the hands at rest, cyanosis is more frequently noted Numbness of the fingers is not appreciated until the attack has lasted for a considerable period, and it is often this which first attracts the patient's attention Pain, usually described as aching, is a feature of severe attacks, and on cold days may be most unpleasant One of the patients in the present series was reduced to tears by the pain, and several described an associated feeling of nausea

During recovery the digit is invaded gradually from base to tip by a red flush, and the march of the redness is easily observed as there is a sharp transition between the hyperaemic recovered portion of the digit and the cyanosed portion in which the arteries are still in spasm Recovery is accompanied by intense tingling paraesthesiae which may be most disagreeable The phenomenon of intermittent leakage described by Lewis (1929) has also been observed small red spots like those on a plaice appear over the surface of a digit and spread for a small distance only to become cyanosed again Lewis (1929) suggests that this is due to a slight temporary relaxation of the spasm in the digital arteries which allows a small amount of arterial blood to seep through before spasm completely occludes the vessel once more Recovery from an attack is accompanied by a conspicuous rise in the surface temperature of the digit (Fig 47, R M F, and Fig 48) but if intermittent leakage occurs,

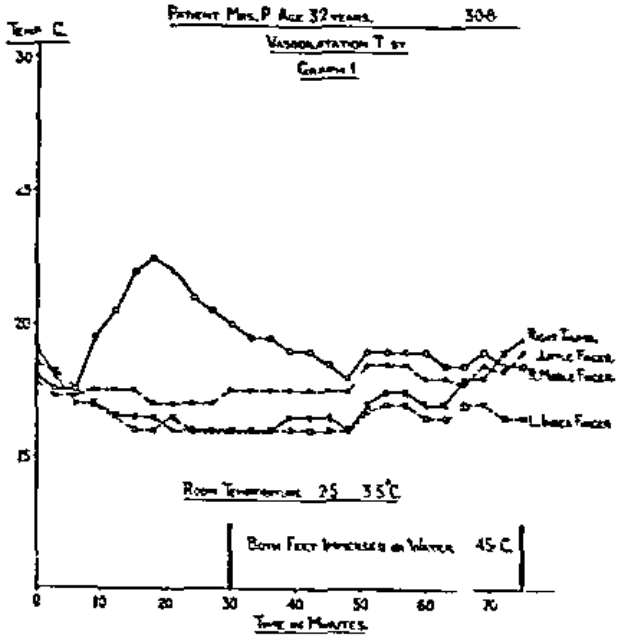

FIG 47

Reflex vasodilatation during attack of Raynaud phenomenon Partial recovery in right middle finger intermittent leakage in left index finger

the temperature does not rise appreciably (Fig 47, L I F)

(2) **Reflex Vasodilatation**—Reflex vasodilatation induced by immersion of the lower limbs in water at 45°C is usually effective in causing vasodilatation in digits which are subject to attacks of the Raynaud phenomenon (Figs 46 and 49) If the digital vessels are in spasm reflex vasodilatation will usually result in a rapid and complete recovery from the attack (Figs 48 and 49) Occasionally if the test is carried out in a cold room the spasm of the digital vessels may be so intense that heating even for 45 minutes may fail to induce a rise in temperature in the fingers (Fig 47) An exceptional type of case is shown in Fig 50 where heating of the lower limbs for 34 minutes

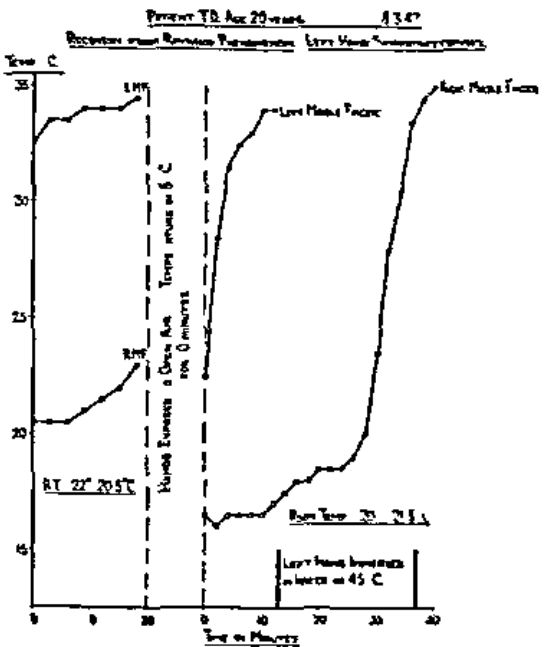

FIG 48

Recovery from attack of Raynaud phenomenon left hand sympath ectomised

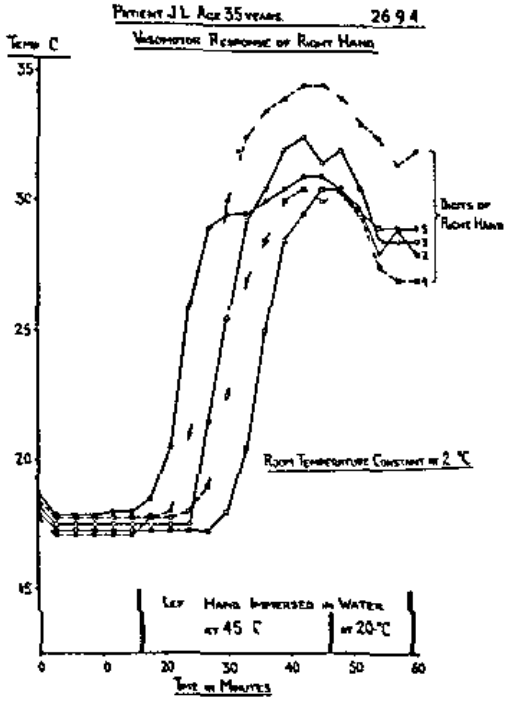

FIG 49

Case JL Reflex vasodilatation to show differences in degree of dilatation in the digits

was required before any rise in temperature in the fingers was observed, but when the vasodilatation did occur, it was rapid and complete In cases where there is a long history of attacks, the ultimate vasodilatation level may fall below that which is considered normal for the fingers In Fig 49 it will be noted that the vasodilatation in the fingers falls below that in the thumb which was unaffected The deficit is greatest in the index which was the digit originally affected, and, at the time of observation, was on clinical grounds judged to be the most severely affected It is considered that this deficit represents a degree of organic narrowing of the digital arteries consequent upon repeated and prolonged attacks of spasm recurring over a long period of time, in this case 10 years

(3) **Nerve Block.**—Lewis (1929) demonstrated that blocking the ulnar nerve did not prevent an attack in the little finger, and that if the ulnar nerve were blocked during an attack, relaxation of the spasm in the digital arteries of the little finger did not necessarily occur In Hunt's (1936a) paper, there is a colour plate (his Fig 14) of the effect of median nerve block upon the Raynaud phenomenon After a right median nerve block the hands were exposed to water at 15°C for 15 minutes The picture shows quite clearly that the area of the right hand affected by the block (the classical median nerve territory) has been unaffected by the cold, whereas the little finger and all digits of the left hand are in a typical attack of local asphyxia Johnson (1941) describes two cases in which median nerve block failed to prevent or relieve attacks of the Raynaud phenomenon

Case JC (Group E) seemed to offer an excellent opportunity of testing the effect of nerve block, since the attacks were confined to the territory of the right median nerve In this case in a warm room it was found necessary to cool the hand to the unusually low temperature of 8°C before

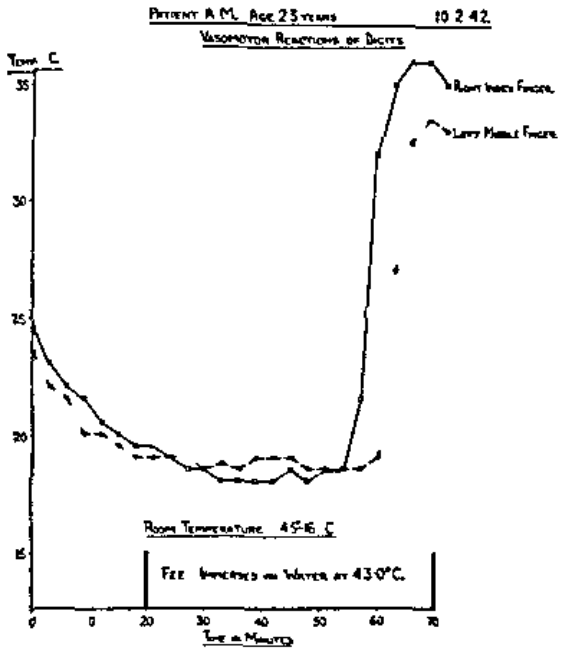

FIG 50

Case AM Reflex vasodilatation note delay before vasodilatation occurs

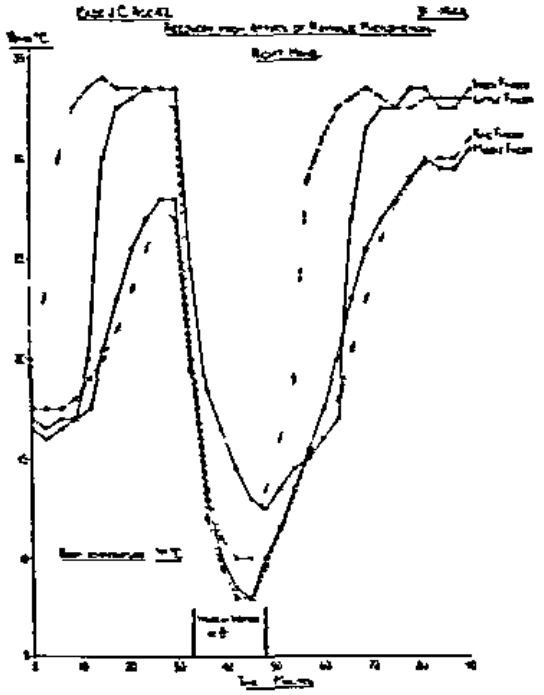

FIG 51

Case JC Right hand—induction of and recovery from an attack of the Raynaud phenomenon

the characteristic clinical features of an attack were observed In Fig 51 recovery from an attack on entering a warm room is followed by the induction of a second attack, followed again by recovery It will be noted that in the recovery from both attacks, the middle and ring fingers show a much slower rate of warming than the index, the unaffected little finger warming almost immediately Fig 52 demonstrates the effect of median nerve block On this occasion, before the test commenced the patient had been allowed to acclimatise to the room temperature As a result, although the fingers were cool, the digital arteries were not in spasm Blocking the median nerve resulted in a typical rise in temperature in the index and middle fingers, and a slight rise in the ring finger The hand was then cooled as on the previous occasion At the end of the period of cooling, the index and middle fingers were reddish in colour, but the tip of the ring finger was cyanosed It will be noted that the rate of warming of the index and middle fingers was appreciably more rapid than before the nerve block After all digits were thoroughly warm, it was found that the nerve block was still effective, and the patient was therefore sent out of doors for 10 minutes It was a cold, windy day, and earlier within a few minutes of going outside, the patient had experienced a typical attack On the present occasion, at the end of the 10 minute period the index and middle fingers were warm and of normal colour, the ring finger was slightly blue at the tip and cool, the little finger was normal in colour and cold In this case therefore, the median nerve block appeared to be effective in preventing an attack in the index and middle fingers but not in the ring finger It should be noted that the attacks were never observed to affect more than the tip of the latter digit

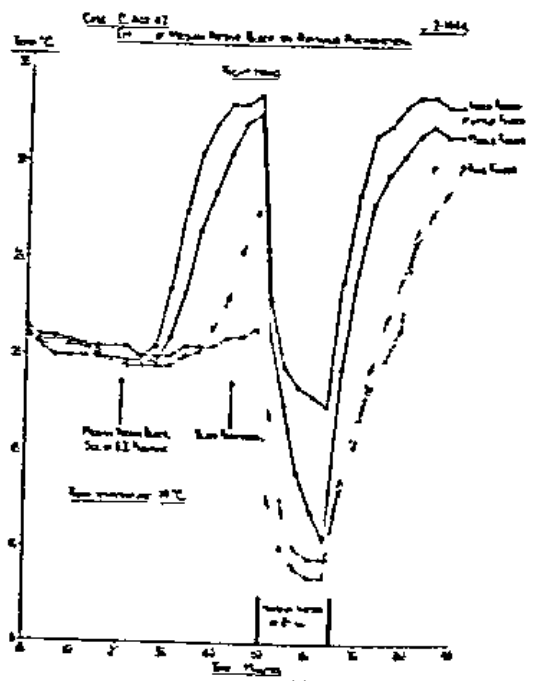

FIG 52

Case JC Right hand—to show effect of median nerve block

PATHOLOGY

Opportunities for obtaining pathological material from cases exhibiting the Raynaud phenomenon are not frequent, since it is very rare for the disease itself to be fatal, and massive gangrene of the digits leading to amputation is uncommon In one case where the fingers were amputated because of gangrene, Spurling *et al* (1932) observed thickening and fibrosis of the intima and hypertrophy of the media They state that the large digital arteries are involved more than the arterioles Lewis (1938a) studied the changes in the arteries of the hand and digits in 6 cases of Raynaud's disease, and compared these with similar arteries from 18 patients who were known not to have had attacks during life He found that in those cases which had exhibited only attacks of discoloration of the digits, the digital arteries showed intimal hyperplasia but this was no more pronounced than in controls belonging to the same age group In cases exhibiting nutritional lesions in the form of necroses or healed necroses of the finger tips, the lumina of the vessels were reduced or occluded by new cellular tissue or by recent or organised thrombus Lewis suggested that in a considerable proportion of cases experiencing attacks of discoloration leading up to necrosis of the finger tips, the initiating factor may very probably be a thrombotic event He found no evidence of muscular hypertrophy, and suggested that previous observers had not realised the thickness of the media of the normal digital artery

In the present series it was possible to examine the digital vessels in one case —

Case MW (*Group B*) Age 46 Two years' history of typical attacks of the Raynaud phenomenon accompanied from the outset by recurrent ' whitlows " which were very painful and always took a long time to heal On admission to hospital there were healed necrotic areas on the left index, middle and ring fingers, and on the right ring finger Typical attacks of the Raynaud phenomenon were frequently observed A vasodilatation test by the limb immersion method was carried out on 13/1/42, and the right ring finger reached a temperature of 34°C On 20/4/42 a right preganglionic cervical sympathectomy was performed At the time of operation the right ring finger showed a small active area of necrosis at the tip This rapidly became worse after the operation, the terminal phalanx of the finger became blue, then black and was causing considerable pain This phalanx was therefore amputated on 11/5/42, at the same time as a left preganglionic sympath

Fig 53
Case MW Photomicrograph showing cross section of digit (x 5)

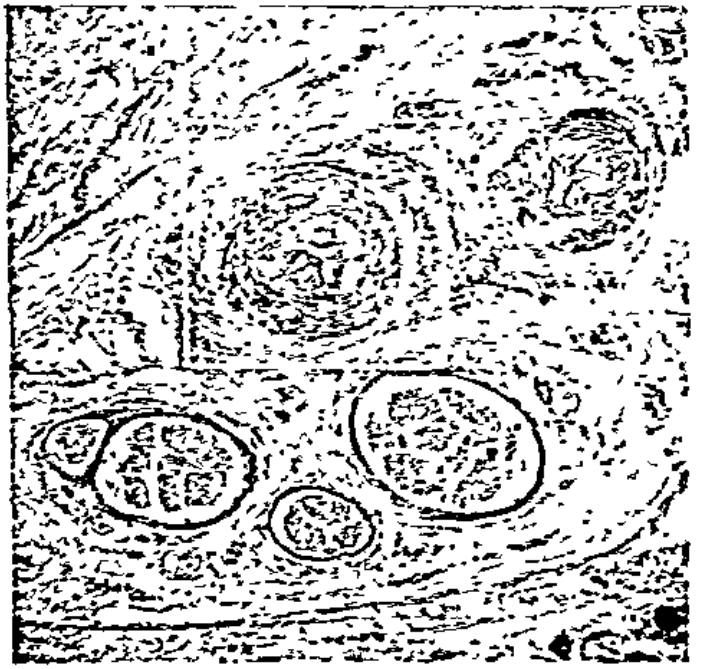

FIG. 54
Case MW. Photomicrograph of digital neurovascular bundle. (x 35)

ectomy was performed. The amputation stump did not heal and the rest of the finger was formally amputated at the metacarpo-phalangeal joint on 5,6,42. Figs. 53-55 show a cross-section of the proximal phalanx, a view of one digital neuro-vascular bundle and a cross-section of the digital artery. The following is an extract from the pathological report for which I am indebted to Dr. R. F. Ogilvie :—

"The subcutaneous tissues are irregularly infiltrated with round cells, mainly plasma cells, in large numbers. In addition, many of the arterioles are unusually thick walled and narrow of lumen owing to a variable increase in the thickness of their intimal coat. Sometimes indeed this endarteritis is so marked that the lumen is scarcely

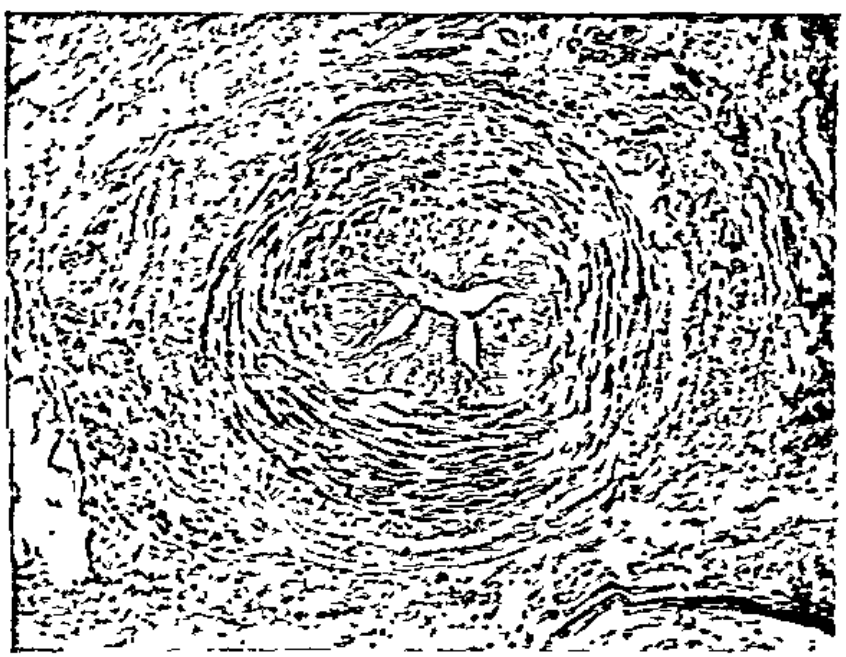

FIG 55
Case MW. Photomicrograph of digital artery. (x 100)

discernible. The thickened intima is occasionally infiltrated with round cells, and in one or two such cases round cells in very small numbers are present among the

muscle fibres of the media The previously narrowed lumen of one arteriole had been finally occluded by thrombus Again, at one side of the largest artery in the section, the formation of granulation tissue including some iron-pigment suggests organisation of a previous clot Finally, in several regions throughout the tissue, granulation tissue is also in process of development The features are those of a chronic inflammatory condition undergoing organisation and involving particularly endarteritis and thrombosis of the arterioles "

These findings are very similar to those described by Lewis, and support his hypothesis that in the presence of necrosis of the finger tips a thrombus is present in the lumen of the digital arteries It is of interest also to note that gangrene of the finger tip occurred even although only one of the main digital arteries was completely occluded In another case which the writer remembers seeing as a student, there was complete occlusion and recanalisation of the digital artery of a little finger [1]

THE EFFECT OF SYMPATHECTOMY

In the present series, preganglionic sympathectomy has been performed in 14 cases It has not been possible to follow all these cases or to make accurate post-operative observations upon many, but a few cases have been studied, some for as long as 2 years after operation, and the present observations are based upon these. The operation has been performed by the posterior approach and is substantially that described by White and Smithwick (1942) It is the author's belief that to obtain the best results, a sympathectomy must be preganglionic and must be complete It is known that several of the cases considered here were incompletely sympathectomised, but at present it is not proposed to enter into a discussion regarding the best type of operation or the reasons for the failure of certain sympathectomies It is considered that the results in the present series may be taken as fairly typical of those likely to be obtained by any competent surgeon who performs the operation for the relief of attacks of the Raynaud phenomenon

In the first place it must be stated that observations in all the present cases confirm the findings of Lewis (1938b) and Fatherree *et al* (1940) that preganglionic sympathectomy does *not* abolish attacks of the Raynaud phenomenon It does, however, relieve nearly all cases Following sympathectomy, the attacks are less frequent, do not last so long, recovery takes place more rapidly (Fig 48), and, most important of all, they are much less painful The amount of relief afforded is not the same in all cases, and depends upon the severity of the attacks before operation As Lewis (1938b) states, if a series of cases exhibiting the Raynaud phenomenon are graded according to severity before and again after operation, it is found that relative to each other they retain the same position on the scale of severity, although post-operatively each will be placed a little lower

The results of sympathectomy are illustrated by the following cases —

Case AA (Group B) A housemaid, aged 41, gave a history of typical attacks of the Raynaud phenomenon for 20 years The attacks had been gradually increasing

[1] *Photomicrographs of this case are reproduced by White & Smithwick (1942).*

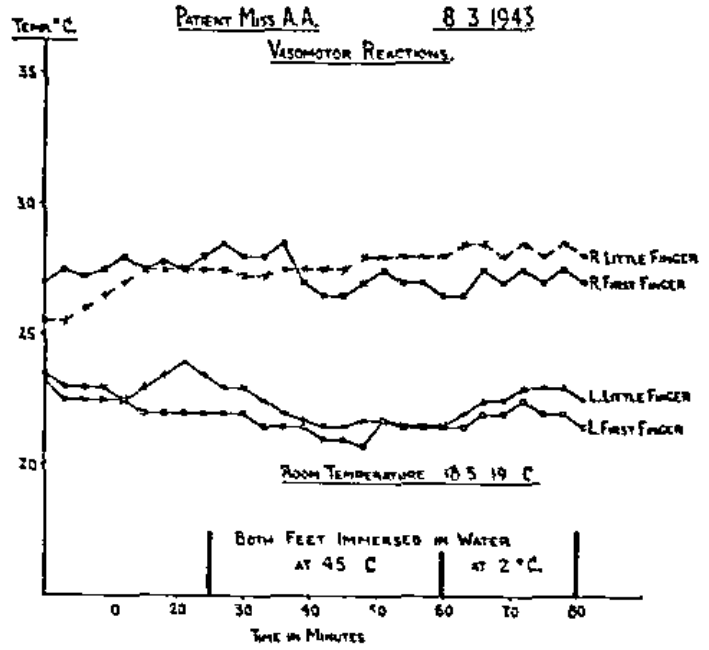

FIG 56

Case AA Vasomotor reactions after preganglionic sympathectomy note difference in temperature of the hands and absence of reflex responses

in frequency and severity, and shortly before her admission to hospital, she had developed small necroses on the tips of the fingers which had taken a long time to heal A left preganglionic sympathectomy was performed on 8/2/43, and the right side was operated upon 8 days later The results of a vasomotor test performed on 8/3/43 are shown in Fig 56 The right hand was now warm, but it was still possible to induce attacks in the digits, the left hand was rather cold and attacks were relatively easily induced Six months after the operation she stated that the right hand was always warm, and that if the fingers did become blue, the attack lasted for only a few minutes, the left hand, however, was cold, attacks were fairly frequent, and chilblains had developed on the digits on several occasions She considered that both hands had been improved by the operation A year after the operation she was still satisfied with the result, although neither hand was free from attacks The result in the right hand was still better than that in the left This difference in the two hands was attributable to a difference in operative technique

Case JC (Group E) Details of this case have been presented above (p 74) and the results of blocking the median nerve described (p 78) A right preganglionic cervical sympathectomy was performed on 25 2 44 Five weeks after operation an attack in the right middle finger was induced by immersion of the hand in water at 13°C (Fig 57) The rate of recovery from this attack is similar to that observed in the same digit before

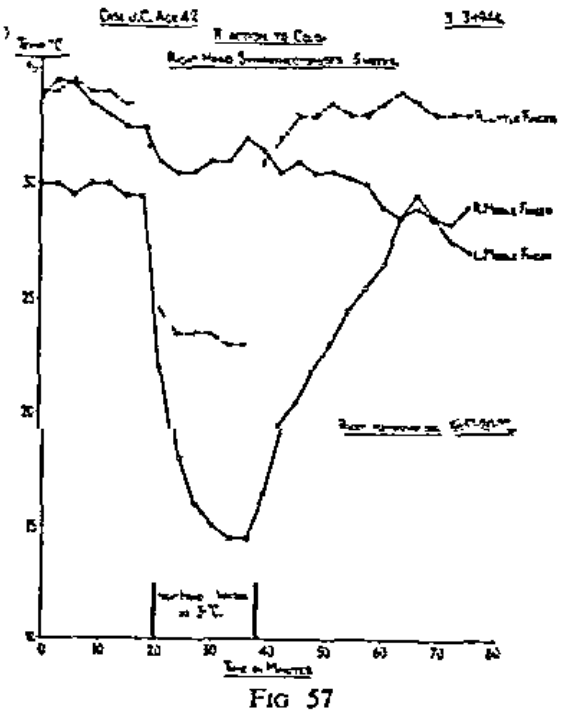

FIG 57

Case JC Right hand five weeks after preganglionic sympathectomy, induction of attack of the Raynaud phenomenon in the middle finger on exposure of the hand to cold

operation (Fig 51) It will be noted that the unaffected little finger cooled little, if at all, during the exposure of the hand to cold Four weeks later, in a cool room, immersion of the lower limbs in hot water failed to induce reflex vasodilatation in the sympathectomised digits (Fig 58) This indicates that the sympathectomy is probably complete, and yet the temperature of the middle finger remained low throughout The patient stated that his attacks were less severe and much less disabling than before the operation , he was pleased with the result

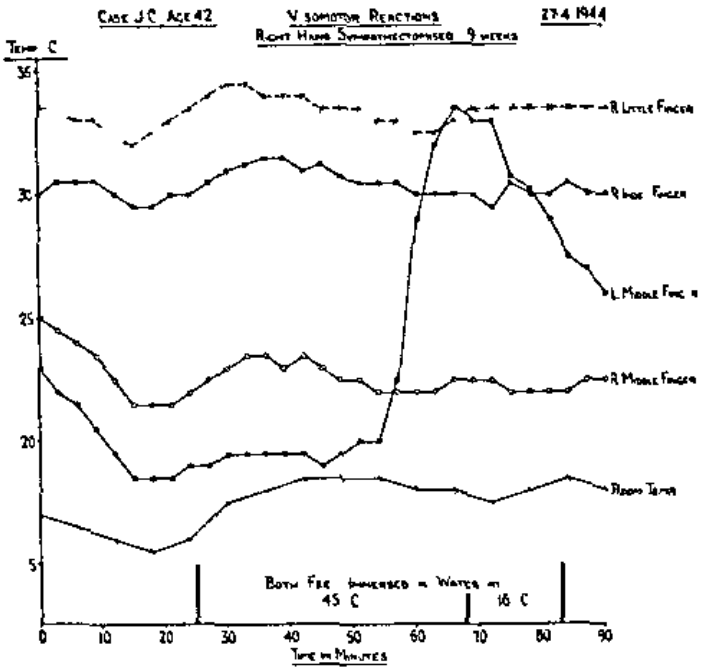

FIG 58

Case JC Vasomotor reactions nine weeks after right preganglionic sympathectomy , note difference in temperature of digits of right hand which shows no reflex vasomotor activity

These examples are sufficient to demonstrate that *preganglionic sympathectomy does not effect a cure in cases exhibiting the Raynaud* phenomenon From a critical viewpoint, the results are disappointing, but it must be admitted that " whatever the problems connected with it may be, sympathectomy is the most satisfactory method of treatment of Raynaud's disease " (Fatherree *et al* , 1940)

DISCUSSION

In his original thesis, Raynaud (1862) stated that attacks of local asphyxia were due to spasm of the arteries in the digits This view has been generally accepted, and subsequent clinical observation and research have amply confirmed it The attacks are due to closure of the main digital arteries , the larger vessels, arterioles *and veins are not primarily involved except in so far as they react normally to the* external stimuli which provoke an attack

Raynaud's hypothesis that the spasm of the digital vessels was the result of an abnormality of the vasomotor nervous system has not met with general acceptance After remaining undisputed for 60 years, it was challenged by Sir Thomas Lewis (*locis cit*) who, as a result of a long series of careful clinical researches, sponsored the hypothesis that attacks of the Raynaud phenomenon are the result of a " local fault " in the digital arteries themselves The precise nature of the " local fault " is unknown, but it results in an unusual reactivity in the wall of the digital artery Lewis's hypothesis is generally accepted in this country, but in America and on the Continent many clinicians are not prepared to accept that the " local fault " hypothesis is applicable to all cases Simpson *et al* , (1930 and 1931), Homans

(1939) and White and Smithwick (1942) maintain that in many cases an abnormality of the sympathetic system is the predominant feature Only recently Hyndman and Wolkin (1942) have published in America a paper in which they support Lewis's hypothesis that Raynaud's disease is primarily an arterial condition Livingston (1935) believes that in the early stages of Raynaud's disease the fundamental disturbance is central and that the vasomotor nerves are involved only in so far as they act as the conducting mechanism In France, Leriche (1939) also maintains that Raynaud's disease is a malady of the sympathetic nervous system, but suggests that certain cases may have a basis in endocrine dysfunction Even Lewis (1936) agrees that the vasomotor nerves have a certain amount of influence, and that impulses passing along these from higher centres may be operative in initiating, prolonging or terminating an attack, provided the local circumstances are otherwise favourable The greatest argument centres round the early case of the Raynaud phenomenon All are prepared to admit that once attacks have been present for some time, local changes may develop in the digital arteries It is more difficult to be certain whether the initial attacks are the result of a local vascular or central vasomotor abnormality

Lewis (1936) bases his "local fault" hypothesis on the following facts —

(1) The digital arteries alone are involved
(2) Local cooling of a hand or digit will induce an attack in that hand or digit alone even if general vasoconstriction is inhibited by warming the body, if the affected hand be kept warm, cooling the body will not produce an attack
(3) Nerve block fails to prevent attacks or to abolish an already established attack
(4) Sympathectomy does not effect a cure nor does it reduce all cases to a common level as it ought to do if Raynaud's disease were a malady of the sympathetic system
(5) Vasoconstrictor tone is higher in the feet than in the hands, but the Raynaud phenomenon is more common in the fingers

In the present study these facts, with the exception of that relating to nerve block, have been confirmed It is considered that the exception offers no bar to the general acceptance of Lewis's hypothesis It appears to the author that no explanation other than a local arterial lesion can explain all the features of the Raynaud phenomenon

Johnson (1941) from a careful study of the digital circulation in 22 cases showing the Raynaud phenomenon, has presented an alternative local vascular mechanism as the cause of the attacks He suggests that the closure of the digital arteries is not an active process but is a passive response to vasodilatation in the palmar arches and diversion of blood from the digits, the digital arteries collapsing as a result of a local fall in blood pressure The evidence upon which he bases this hypothesis is as follows

(1) During attacks the radial pulse remains unaltered
(2) He has proved that under certain circumstances blood may be diverted from the digits amyl nitrite diverts blood from the digits to the splanchnic area with a fall in blood pressure and constriction of the digital arteries

(3) Median nerve block causes a conspicuous rise in temperature in the thumb, index and middle fingers and a slight rise in temperature in the ring finger but causes a *fall* in temperature in the little finger and in one case blocking the median nerve caused a typical Raynaud attack in the little finger only

He finds that patients who suffer from attacks of the Raynaud phenomenon have a reduced digital circulation even between attacks and believes that in such cases less blood will have to be diverted from the digits to cause the digital arteries to collapse than in a normal person. The greater the reduction in blood flow between attacks the greater the liability of the digital arteries to go into spasm, patients with organic vascular disease suffer more severely than others. A point in favour of this hypothesis is that some patients complain that attacks are more frequent after meals. Unless it can be proved that vasodilatation in the palmar arches or elsewhere in the body takes place during Raynaud attacks, the mechanism suggested by Johnson cannot be accepted as applicable to all cases exhibiting the Raynaud phenomenon.

It is important to consider to what extent the Raynaud phenomenon may be considered a pathological process. Monro (1899) puts the problem thus: "Local syncope, the first of the three characteristic stages in a typical case of Raynaud's disease cannot of itself be regarded as a disease so long as it amounts to nothing more than the familiar 'dead fingers'. The condition is in the first instance, as a rule, protective in its nature, the purpose being to cut off the access of blood to those parts that most readily lose heat by radiation, in circumstances where cooling might take place to a degree dangerous to the whole organism. That dead fingers, however, cannot be looked upon as normal is evidenced by the impairment of function and especially of the tactile sensation necessary for the execution of delicate movements, that so constantly accompanies them. *Local syncope is the result not of a normal physiological process, but of the exaggeration of a normal process*." It is difficult, if not impossible, to state at what point the physiological protective reaction becomes a pathological phenomenon, and it is probable that the mechanism responsible for attacks of the Raynaud phenomenon is already present in the normal digital artery.

The relationship of the phenomenon to cold is significant. Cold is not only the precipitating factor in the majority of attacks, but may in some cases be a primary aetiological factor. It has been shown (p. 74) that severe cold may cause a typical attack in apparently normal digits without any subsequent recurrence. Recently it has been realised that the Raynaud phenomenon may be a late sequel of severe and protracted exposure to cold. Case AM (p. 73) is a case in point, and the author has also observed the Raynaud phenomenon as a sequel to "immersion hand" (p. 130). It is of significance also that the histological changes in the arteries in cases exhibiting the Raynaud phenomenon are similar to those recently described by Davis *et al* (1943) in high altitude frostbite. That milder degrees of cold may accelerate the onset of attacks in those already predisposed to them is suggested by the cases described on p. 72. There is, therefore, considerable presumptive evidence that the Raynaud phenomenon, whatever its essential cause, represents an exaggeration of the normal response to cold. Livingston (1935) suggests that "Raynaud's

disease " on the one hand and " erythromelalgia "[1] on the other may be considered as pathological extremes of the normal vasoconstriction and reactionary vasodilatation which follow the exposure of an extremity to cold

Attacks occurring in peripheral vascular disease are assumed to be due to local disease of the digital arteries, thrombosis in these occurs either as a result of local disease of the vessel wall or as a sequel to the lodgment of emboli detached from thrombi in the larger proximal vessels Lewis and Pickering (1934) and Holling (1939) consider that this is also the most likely mechanism for the vascular phenomena of the cervical rib syndrome They reject the hypotheses of Todd (1912 and 1913) and Telford and Stopford (1931) that vasospastic attacks may be the result of irritation of sympathetic fibres in the lowest trunk of the brachial plexus, and believe that emboli are dislodged from a thrombus in the subclavian artery

The relationship of the Raynaud phenomenon to trauma of the vibrating variety has long been recognised In cases of this nature the attacks do not as a rule occur while the patient is working with the vibrating tool, but on exposure to cold as in other varieties of the condition The nature of the disturbance produced by the vibration is obscure, but since the attacks are most severe in those digits which are subjected to the greatest intensity of vibration, it is apparent that the abnormality must be of a local nature

An association between the Raynaud phenomenon and local trauma is less clearly recognised Lewis and Pickering (1934) described a case in which, 4 years after an injury from a fives ball, attacks occurred in a single digit, and Hunt (1936a), a similar case developing 28 years after a whitlow In the present case (JC) the attacks began soon after the injury and were not confined to the injured digit Grant (1935) has suggested that if local disease precedes the Raynaud phenomenon, the latter may be the result of local interference with the nerves of the blood vessels In the case under discussion the attacks were limited to the distribution of the median nerve, an observation which is very suggestive of an underlying nervous abnormality It is very difficult to see what form this abnormality could take If a mechanism of this nature exists, the Raynaud phenomenon might be expected to occur as a sequel to lesions of the peripheral nerves In a large series of peripheral nerve injuries the author has neither witnessed nor heard of a typical attack of the Raynaud phenomenon Doupe (1943a) has recently considered the relationship between the vasomotor disorders that follow nerve injury and the Raynaud phenomenon, and has concluded that there is no correlation between the two It is also pertinent to consider why in the present case nerve block was effective in preventing an attack, whereas an apparently complete sympathectomy was not Two possibilities may be suggested —

(1) That nerve block, being an acute process, resulted in no denervation sensitivity in the affected blood vessels Sympathectomy, even when preganglionic, does cause such sensitivity (Fatherree *et al*, 1940, Doupe, 1943b) Fatherree and Allen

[1] A chronic disease in which a part or parts—usually one or more extremities—suffer with pain, flushing and local fever made far worse if the parts hang down (Weir Mitchell quoted by Osler, 1903)

(1938) have shown that the Raynaud phenomenon is not the result of sensitisation of the digital arteries to adrenalin, but this does not exclude the possibility that, after sympathectomy, adrenalin release may be sufficient to initiate an attack of spasm in vessels in which a " local fault " is already present

(2) Non-sympathetic fibres running in the peripheral nerves may be involved in the mechanism of the Raynaud phenomenon These would be interrupted by nerve block but not by sympathectomy The possibility that somatic nerve fibres may play a part in the causation of the Raynaud phenomenon has also been considered by Johnson (1941) At present this problem is unsolved, but it is interesting to speculate what would happen if a patient subject to attacks of the Raynaud phenomenon had the misfortune to suffer an injury to his ulnar or median nerve Would the attacks cease in the totally denervated digits ?

The present case (JC) offers strong presumptive evidence that the " local fault " responsible for the Raynaud phenomenon may be related to the nervous control of the digital arteries, but it does not help to elucidate more fully the nature of this " local fault "

SUMMARY

A series of observations on cases exhibiting the Raynaud phenomenon are described The observations are largely confirmatory of those previously carried out by Sir Thomas Lewis, and support his hypothesis that in the majority of cases the Raynaud phenomenon is the result of a " local fault " in the digital arteries themselves The nature of this " local fault " remains obscure, but evidence is presented in favour of the suggestion that in some cases it may be related to the innervation of the arteries

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CHAPTER SEVEN

PERIPHERAL NERVE INJURIES[1]

INTRODUCTION

IN the peripheral nervous system of man there is no grouping of nerve fibres according to function It follows that complete division of a peripheral nerve, however caused, will produce a state in which the effects of motor paralysis, of loss of sensation and of autonomic dysfunction are closely intermingled If the nerve division be incomplete, it is possible to postulate a state of affairs in which motor and/or sensory fibres might be interrupted, either completely or incompletely, and autonomic fibres escape In studying the complex effects of peripheral nerve lesions, it must be realised that it is impossible completely to dissociate those produced by division of autonomic fibres from those produced by division of motor and sensory fibres, and both disuse and therm anaesthesia, leading to disregard to extremes of temperature, play their part in the production of cutaneous vasomotor disturbances

Efferent autonomic nerve fibres to the limbs include three groups sudomotor, pilomotor and vasomotor A study of the disturbances of sweat secretion following peripheral nerve injuries has been made elsewhere (Guttmann, 1940, Highet, 1943) Disturbances of pilomotor function were described very accurately by both Head and Sherren (1905) and Trotter and Davies (1909) In this communication observations on the vasomotor disturbances which follow lesions of the main nerve trunks of the limbs will be recorded

PREVIOUS OBSERVATIONS

Waller (1861 62) investigated the effects of freezing and compression upon peripheral nerves Temperature changes in the affected area were recorded with a sensitive mercury thermometer He found that refrigeration of the ulnar nerve caused a rise in temperature in the interdigital cleft between the ring and little fingers, prolonged pressure upon the ulnar nerve caused a fall in temperature In their classical monograph, "On Gunshot Wounds and Other Injuries of Nerves," Weir Mitchell, Morehouse and Keen (1864) devoted a chapter to "The Condition of Calorification in Injuries of Nerves" They were able to demonstrate that the surface temperature of an area deprived of sensation was uniformly lower than that of the corresponding area in the normal limb, the exceptions to this rule were those cases with the "burning pain" which they later named "causalgia" In this country, Hutchinson (1866) noted that after a peripheral nerve injury there "was always a

[1] Some of the observations recorded in this chapter have already been published (Richards 1943)

remarkable loss of heat in the part which has lost sensation" This coldness he attributed to a disturbed capillary circulation as a result of alterations in cell metabolism In the early years of this century, the researches of Head and Sherren (1905) and Trotter and Davies (1909) added much to our knowledge of the effects which follow the division and attend the recovery of peripheral nerves Both these groups of observers were concerned chiefly with problems of sensation, but also described the changes which take place in the skin of a denervated area Head and Sherren did not separate sudomotor and pilomotor effects from vasomotor, Trotter and Davies gave an account of the vasomotor disturbances which took place in cutaneous areas deprived of sensation All the nerves which they chose for their experimental work supplied the more proximal portions of the limbs, and probably contained few vasomotor fibres Later Sharpey Schafer (1928) studied the effects of denervation upon the little finger of his left hand Like the previous observers, he was concerned chiefly with sensory phenomena, but mentioned that the finger was colder than the normal finger of the right hand and that nail growth was slower than normal

During the last war the study of injuries to the main nerve trunks of the limbs provided much new diagnostic and prognostic information about sensory and motor disturbances The vasomotor disorders seem to have been somewhat neglected except when they were accompanied by other disturbing features such as the pain of causalgia (M R C Report, 1920, Thorburn, 1922) Benisty (1918) stated that vasomotor, "trophic" and secretory disturbances appeared "only in cases where there is an arterial lesion in addition to the wound of the nerve" In Germany, Breslauer (1919) published a long and involved paper on "The Pathogenesis of Trophic Tissue Damage after Nerve Injury" He stated that immediately after gunshot wounds of the peripheral nerves the cutaneous circulation was unaltered The late effects of a nerve injury upon the circulation in the anaesthetic area were either "anaemia" in which the skin was pale, dry and brittle or "venous hyperaemia" in which the skin was shiny and bluish red or deep blue in colour He investigated the reaction of the denervated tissues to trauma and found that immediately after nerve section such tissues retained the power to react normally to noxious stimuli but after a few weeks, active hyperaemia, the first stage of inflammation, could no longer be elicited Vasoconstriction in response to cold and the *reactionary vasodilatation which follows were unaffected as was vasoconstriction in* response to the local injection of adrenalin He concluded that the "trophic" tissue damage which may follow nerve injury was due to a disturbed circulation and that the integrity of the peripheral nerves was necessary for the normal course of inflammation

Since the last war, outstanding advances have been made in our knowledge of the form and functions of the autonomic nervous system The surgical operation of sympathectomy has become a recognised therapeutic procedure, and as a result a better understanding of the effects of pure lesions of the autonomic nerves has enabled a more rational approach to be made to the problem of the so-called trophic' changes which may accompany peripheral nerve injuries Lewis and

Pickering (1936) undertook an investigation into the circulatory changes which occur in digits in diseases of the nervous system A careful study of many types of lesion ranging from musculo-tendinous injuries, which produced immobility and disuse without interfering with the digital nerve supply, to peripheral nerve injuries, led them to conclude that all the effects of nerve division could be attributed to interruption of motor, sensory and autonomic nerve fibres, and that there was no reason to postulate the existence of a separate set of nerve fibres which exerted a 'trophic" influence on the skin and its appendages Thus the term " trophic " has no accepted physiological explanation and will not be used

MATERIAL

The material upon which the present study is based consists of a series of some 350 patients exhibiting lesions of the main nerve trunks of the limbs who were admitted to a Scottish peripheral nerve injury centre during the period June 1941 to March 1944 Not all cases were subjected to a vasomotor investigation, but it is considered that the observations herein reported are a fair representation of what may be found in a group of unselected peripheral nerve lesions

Classification of Material —*The classification of nerve injuries has always been* a matter of some difficulty Recently Seddon (1942 and 1943) has proposed a grouping into cases of 'neurotmesis" (complete anatomical division), " axonotmesis' (the so-called " lesion in continuity " in which the nerve fibres are divided but the supporting structure remains intact), and " neurapraxia " (a ' transient block " *in which paralysis without Wallerian degeneration results and recovery is* rapid and complete) This is a very exact classification based upon anatomical and physiological principles, but its value for everyday clinical use is doubtful For the purposes of the present study, cases have been divided into two groups complete division and incomplete division Cases were placed in the first group only when the nerve was seen to be divided at operation, or if a consideration of *all* the clinical findings left no doubt as to the diagnosis all other cases were considered to belong to the second group In the first group the clinical manifestations are those of loss of function , in the second group those of perversion of function may be superadded The extreme example of perversion of function is causalgia Recovering lesions of *peripheral nerves present certain unique problems and require separate consideration* Any case with evidence of an associated vascular lesion has been excluded so that the results might be interpreted in terms of *nerve function alone Since there are* differences between the vasomotor responses of the upper and lower limbs, it is advisable, at least in the first instance, to consider each separately

COMPLETE NERVE DIVISION

The distribution of vasomotor nerve fibres has been shown to be predominantly peripheral (p 10) This anatomical arrangement explains why vasomotor disturbances may be very noticeable in the hand or foot if median, ulnar or sciatic nerve be divided, but *insignificant in the more proximal portions of the limbs after division*

of such nerves as the medial cutaneous nerve of the forearm or lateral cutaneous nerve of the thigh There is also a physiological explanation for this apparent anomaly Grant and Holling (1938) have shown, and recently Doupe *et al* (1943) have confirmed, that the vasomotor innervation of the skin of the proximal portion of the limbs is predominantly vasodilator There is no evidence that vasodilator fibres exert any tonic action upon blood vessels, so that disturbances after division of such fibres will be less pronounced than after interruption of vasoconstrictor fibres

In the present study attention has been directed chiefly to the hand and foot, and observations have been made not only upon the resting vasomotor state of denervated areas,[1] but also upon the extent to which they may show evidence of vasomotor activity

A Upper Limb.

(1) *Vasomotor Effects of Nerve Division*—Immediately after division of a peripheral nerve there is a period of vasomotor paralysis due to release of normal vasoconstrictor tone over the territory to which the divided nerve supplies cutaneous sensory fibres A well defined area of skin, corresponding roughly to that over which there is analgesia to pinprick, becomes hot, flushed and dry During this phase the temperature of the part is still independent of the temperature of its environment In this early stage the characteristic of the skin temperature of a denervated area is its stability (Fig 59) This initial period of vasodilatation is not maintained After a variable period, usually about 21 days, the vasodilatation passes off, and is succeeded by a state of affairs in which the insensitive area is cyanosed and usually colder than the adjacent normally innervated area (Fig. 60) If the nerve is not repaired, the affected area will remain like this and other nutritional changes such as digital atrophy, loss of skin creases, alterations in the growth of the nails, and indolent ulcers will appear The latter picture is more familiar than the former,

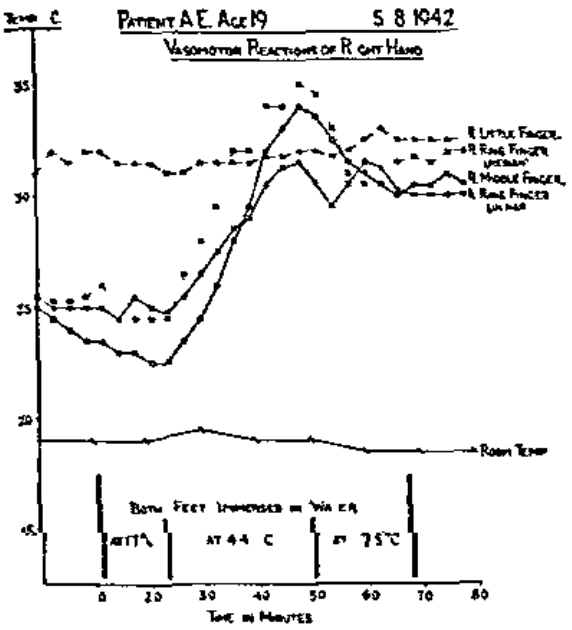

FIG 59
Four weeks after complete division of right ulnar nerve note vasomotor paralysis in right little finger which is still warm

[1] The term denervated applied to an area or a digit is taken throughout to mean that the area referred to is deprived of *cutaneous* sensibility—thus in a complete lesion of the ulnar nerve the little finger will be considered a denervated digit although deep sensibility and appreciation of joint movement may still be present.

because most cases of nerve injury have passed into it before they come under the surgeon's care

During this second stage the skin of the denervated area loses its independence of the environmental temperature, and, if exposed to extremes of temperature, will cool and warm almost like an inert body, a fact which is appreciated by intelligent patients with nerve injuries When questioned about the temperature of denervated fingers, they will reply that when the hand is very warm the insensitive digits are warmer than the others, and when the hand is cool they are colder This "loss of

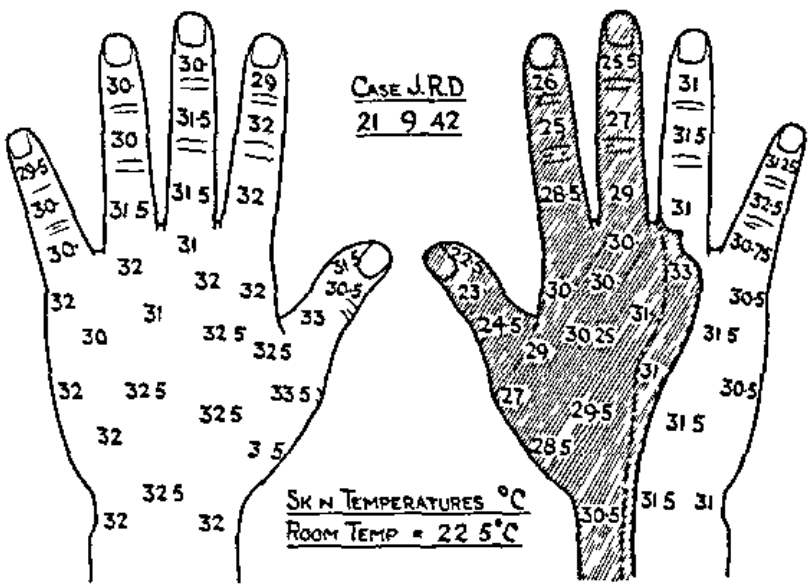

FIG 60
Traction lesion of right brachial plexus note low skin temperature of insensitive area (shaded) compared with adjacent normal area and left hand

independence" in the temperature of a denervated area was noted by Hutchinson (1866) and Trotter and Davies (1909) Hutchinson states "It is a remarkable feature as regards the heat of paralysed parts that it is so much at the mercy of external influences"

There are thus two distinct phases in the resting vasomotor state of an area deprived of its nerve supply (1) an initial phase of vasodilatation which it is proposed to call the 'warm phase,' and (2) a later and permanent phase when the temperature of the area is dependent upon that of its environment Since environmental temperatures in this country are usually low, it is convenient to refer to this later phase as the "cold phase" No clear cut distinction in time exists between these two phases The change is considered to take place within the first three weeks (Lewis and Pickering, 1936) Such investigations as it has been possible to make on cases still in the warm phase when they came under observation, suggest that there is a great variability in the time which elapses between nerve division and the onset of

the cold phase, cases have been seen where the denervated area has remained warm for as long as 6 weeks to three months It has been observed that the tendency for the warm phase to persist is greatest in those cases where denervation of the limb is most complete, that is in complete or almost complete lesions of the brachial plexus

(2) *Effect of Local Temperature*—It has been stated above that in the cold phase the temperature of a denervated area is dependent upon that of its environment In order to substantiate this hypothesis, experiments were conducted to study the effect upon the hand of variations in local temperature For this purpose the hand

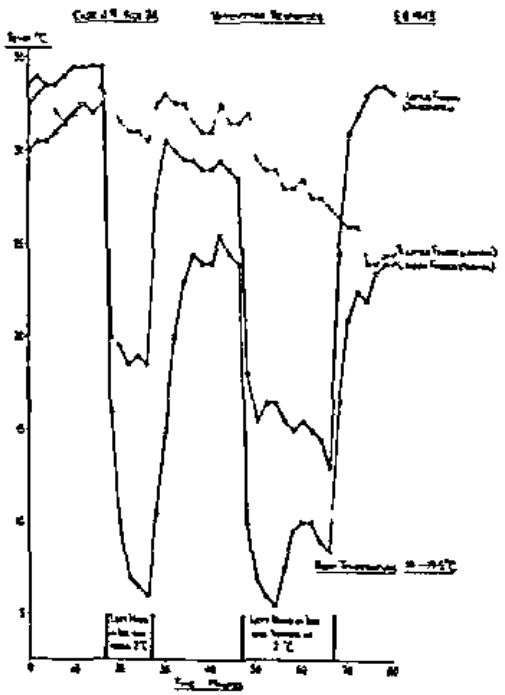

FIG 61

Fourteen days after complete division of ulnar nerve to show reaction to low temperature of denervated digit

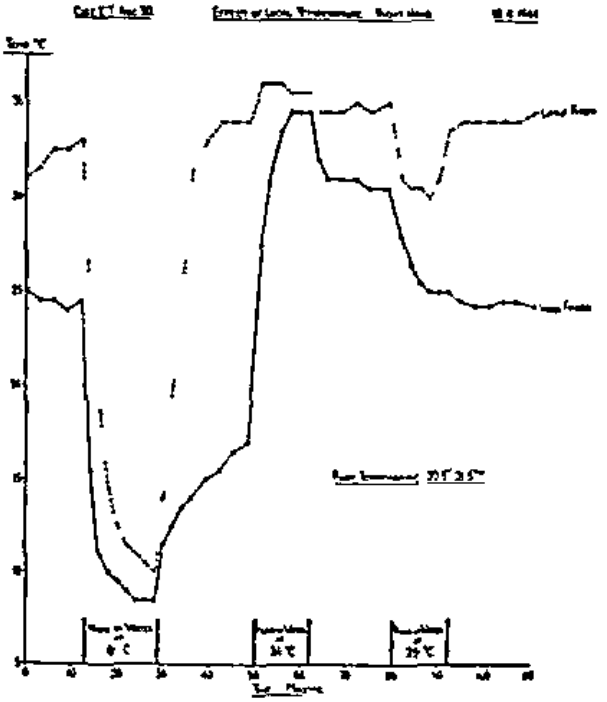

FIG 62

One year after division of right median nerve to show the effect of local temperature upon denervated and normal digits

with thermocouples attached to the digits was covered with a surgeon's rubber glove and then immersed in water at the desired temperature Temperature readings were continued during the period of immersion Immediately the hand was taken from the water, the glove was removed

The effect of exposing the left hand to cold 2 weeks after division of the left ulnar nerve is shown in Fig 61 The little finger was still in the warm phase and when cooled initially for 10 minutes the temperature fell to only 18 5°C, whereas that of the normally innervated digit fell to 6°C Since, during the period of exposure, the thermocouple readings represent a resultant between finger temperature and water-bath temperature (2°C), this indicates that there was little or no vasoconstriction in the denervated digit On exposing the hand for a second and more prolonged period, the denervated digit cooled to 12 5°C On this occasion between 7 and 15 minutes

after exposure to cold, the normal digit showed a conspicuous vasodilatation, there was a slight suggestion of a similar reaction in the denervated digit In the denervated little finger the after-reaction to cold following the second exposure was more pronounced

Once the cold phase has been reached, the reaction of denervated digits to local changes in temperature is much less paradoxical Fig 62 demonstrates the effect of exposure of the right hand to various temperatures 12 months after division of the median nerve The denervated index finger is initially colder than the normally innervated little finger While exposed to cold, both cool to the temperature of the water, thereafter the normal digit warms rapidly to almost full vasodilatation level, but the denervated digit warms very slowly towards room temperature The hand is now warmed and both digits become warm, the denervated digit tends to retain its warmth, but when brought in contact with cool water with its greater thermal conductivity, the temperature immediately drops to that of the water and remains there While in contact with the cool water, the warm normally innervated digit cools, but thereafter immediately regains its warmth

These two examples may be considered as typical of the observations in this group During the warm phase denervated digits do not cool on exposure to cold, and in this respect resemble the digits of a hand which has been subjected to a preganglionic sympathectomy Once the cold phase has developed, denervated digits even after a brief exposure to cold exhibit a tendency to remain cold for a considerable period, when warmed they tend to maintain their warmth provided that the rest of the hand is warm If environmental temperature is low so that, by virtue of its thermo-regulatory function, the normally innervated portion of the hand has a low temperature, then after warming, both normal and denervated digits cool slowly towards environmental temperature

(3) *Vasomotor Reflexes after Nerve Division* —When the vasomotor reflexes of a hand to which a nerve has been interrupted are tested by immersion of the lower limbs in hot or cold water, it is found that digits which are denervated show a profound disturbance of their vasomotor activity whether they are in the early warm phase (Fig 59) or in the cold phase (Fig 63) Usually this takes the form of failure of the denervated digit to respond by reflex vasodilatation The responses are never

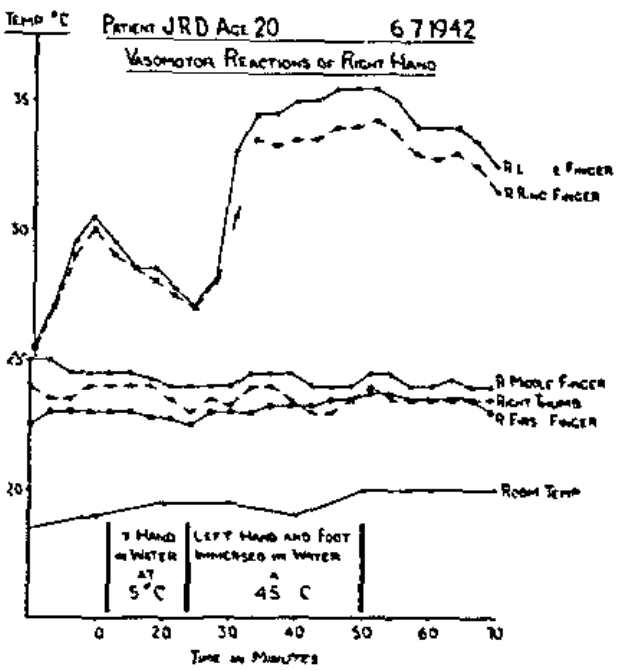

FIG 63

Same case as Fig 60 note absence of vasomotor responses in insensitive digits

absolutely clear-cut, and lesions of the same nerve in different subjects will not give exactly comparable graphs However, it is possible to indicate in a general way the type of response which is to be expected following the interruption of any one particular nerve Thus a typical vasomotor chart from a case of division of the ulnar nerve above the origin of its dorsal cutaneous branch is shown in Fig 64 The index and ring fingers show a normal response The little finger shows very little response, and such response as it does show is delayed and very incomplete compared with that of a normal digit In an isolated lesion of the ulnar nerve, and

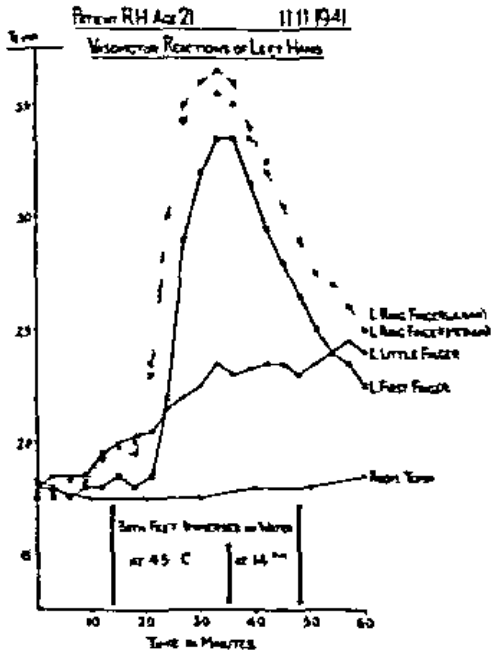

FIG 64
Complete division of left ulnar nerve note normal vasomotor responses in ring finger and slight response in little finger

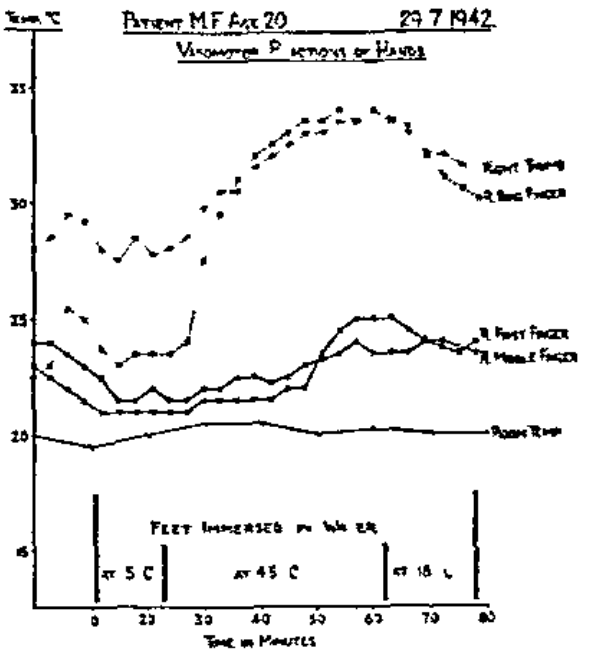

FIG 65
Complete division of right median nerve note normal responses in thumb and ring finger, slight or absent responses in index and middle fingers

sometimes in a median nerve injury, the ring finger is a partly denervated digit In all cases of this nature it has been found that, if thermocouples are attached to both sensitive and anaesthetic sides of the digit, they will record temperatures which do not differ by more than 1 2 C throughout (Fig 64)

In lesions of the median nerve the responses from the thumb and the ring finger are usually almost normal (Fig 65) The index finger does not respond at all The middle finger may not respond or it may, like the little finger in an ulnar lesion, show a delayed response which is slow and incomplete These statements are generalisations based on records made in several cases, and it is rare for an individual case to conform exactly to this vasomotor pattern, for example in Fig 65 the index—not the middle finger—shows a slight response In a median nerve lesion, the response

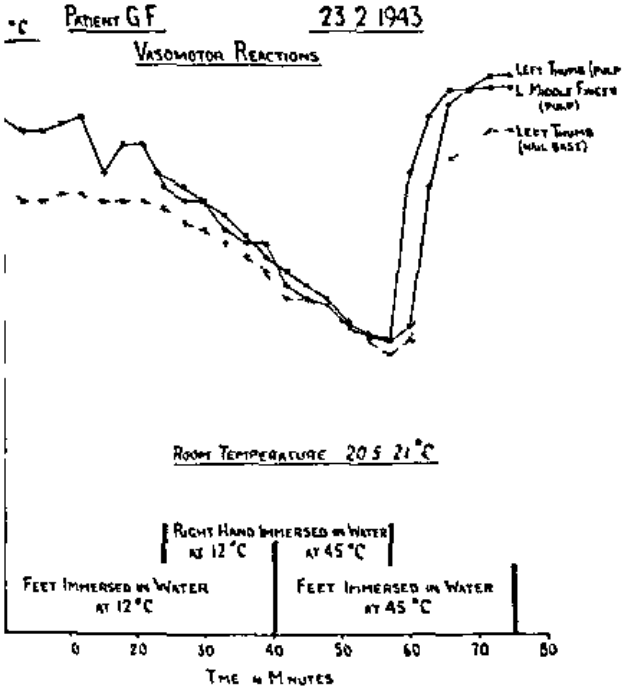

FIG 66
Complete division of left radial nerve, note normal vasomotor response in left thumb

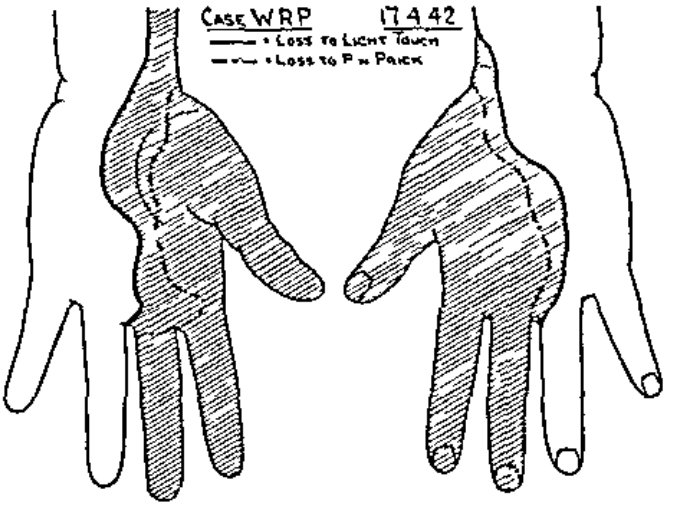

FIG 67
Division of left median and superficial radial nerves in the forearm, to show loss of sensation

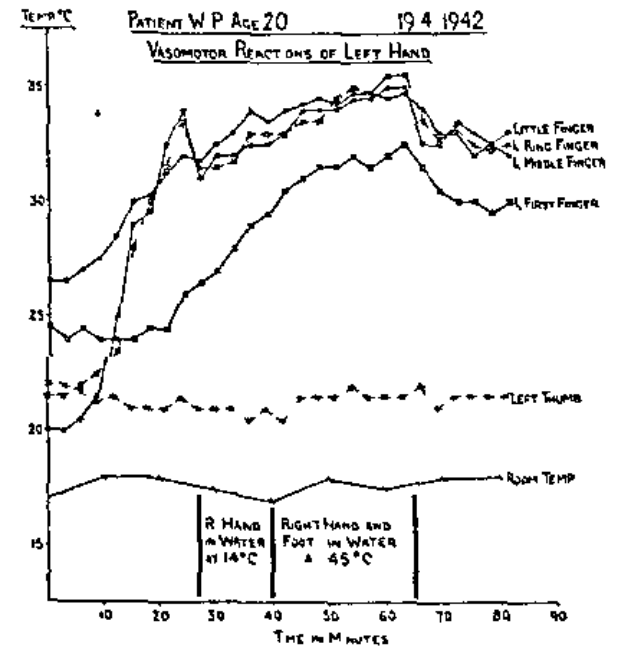

FIG 68
Same case as Fig 67, note absence of vasomotor response in left thumb

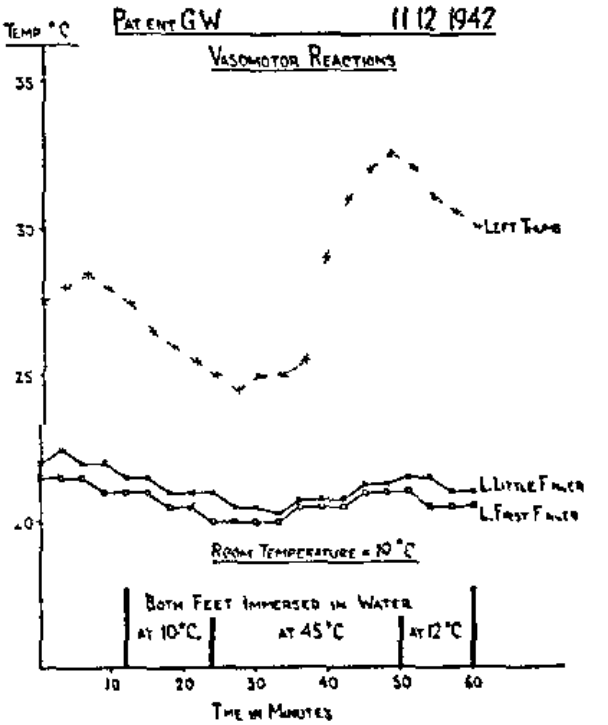

FIG 69
Division of left median and ulnar nerves in the arm, note vasomotor response in the thumb

of the thumb is frequently slower than that of the ring and little fingers, only once has the thumb failed to respond, in a case where the median nerve was injured in the palm (p 117, Fig 91)

From a vasomotor point of view, the thumb is the most interesting digit In a normal hand its resting temperature is usually a degree or two higher, its reflex response is slower, and the final temperature attained is lower than that of the fingers Division of the radial nerve does not abolish reflex vasomotor activity in the thumb, but slight modification of the response may be noted (Fig 66) The absence of vasomotor disturbances in the thumb following division of the radial nerve has also been noted by Philippides (1942) In a case where both median and superficial radial nerves were injured in the forearm, and the thumb became a completely denervated digit, it failed to respond (Figs 67 and 68) In a high lesion involving both median and ulnar nerves, a fair response is obtained in the thumb, but none in the index (Fig 69)

Lesions of the brachial plexus present a more complicated problem because it is more difficult to decide from motor and sensory signs the exact situation of the lesion in the plexus It is possible to recognise certain well-defined types of lesion and to study their effect on the digital vasomotor responses Cases showing signs of damage to the whole plexus, with complete paralysis and loss of sensation below the shoulder, except for the area supplied by the intercosto humeral nerve, do not show a response in any of the digits The Erb-Duchenne type of palsy, in which the 5th and 6th roots are chiefly involved, seems to affect the responses very little Fig 70 is taken from a patient with this type of lesion, who had definite hypaesthesia and hypalgesia of the right thumb and thenar eminence (Fig 71) In lower plexus palsies where the chief damage is to the first thoracic root, the responses are very similar to those from cases of ulnar nerve palsy Fig. 72 shows the responses in a patient who had a very clearly defined lesion of C8 and T1 with a well marked Horner s syndrome There is also the case when the injury is more extensive than that of the Erb-Duchenne type, yet the lower portion of the plexus escaped damage In such a case, a profound disturbance of vasomotor function is noted in the first three digits (Fig 63)

B Lower Limb

(1) *Effects of Nerve Division* —In contrast to the hand, there are five nerves which may carry vasomotor fibres to the foot internal saphenous, musculo-cutaneous, sural anterior and posterior tibial Of these all but the saphenous are branches of the sciatic nerve the saphenous is also the only one which does not normally supply branches to the toes Complete division of the sciatic nerve results in marked nutritional changes in the foot Lesions of the sciatic nerve are the result of more serious and more disabling injuries than wounds affecting the main nerves of the upper limb As a result, it is longer before such cases reach a peripheral nerve centre and the present series contains no case of injury to the sciatic nerve or its branches which has come under observation within 8 weeks of the initial injury

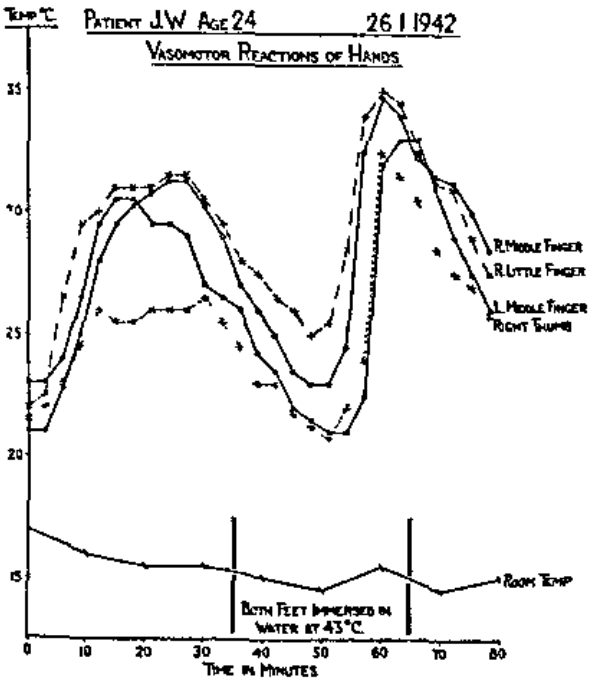

FIG 70
Traction lesion of right brachial plexus (C5 and 6) note normal vasomotor responses in all digits of right hand

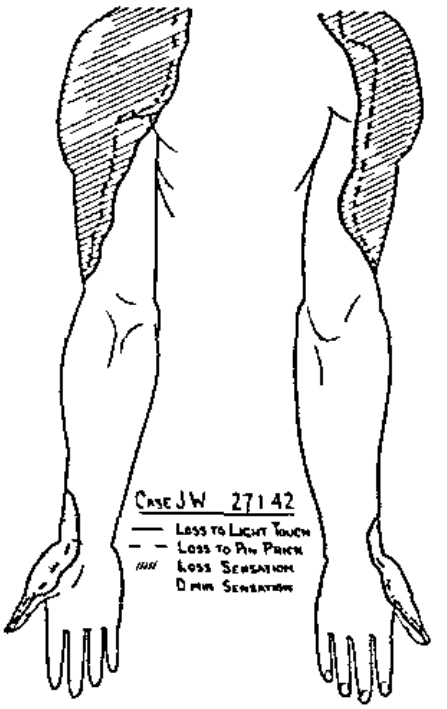

FIG 71
Same case as Fig 70 to show area of sensory loss and hypaesthesia and hypalgesia over the thenar region

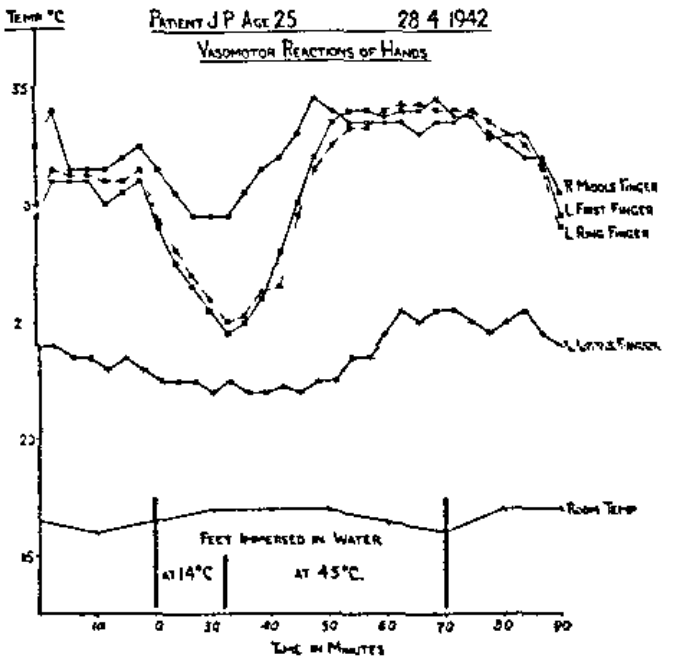

FIG 72
Traction lesion of left brachial plexus (C8 and T1), note abnormal response in little finger only

If the findings in the hand could be transferred to the foot, it would be expected that after this time interval the foot would have entered the cold phase, and indeed a cold, *cyanosed, swollen foot is generally regarded as characteristic of a sciatic nerve palsy* Patients as a rule are inconsistent if questioned about the temperature of the affected foot A common statement is that the foot is usually warm, both objectively and subjectively, but upon occasions feels subjectively very cold although objectively it may not feel colder than the normal foot When patients are in hospital and going about with their feet well protected, the affected foot is invariably warmer than the

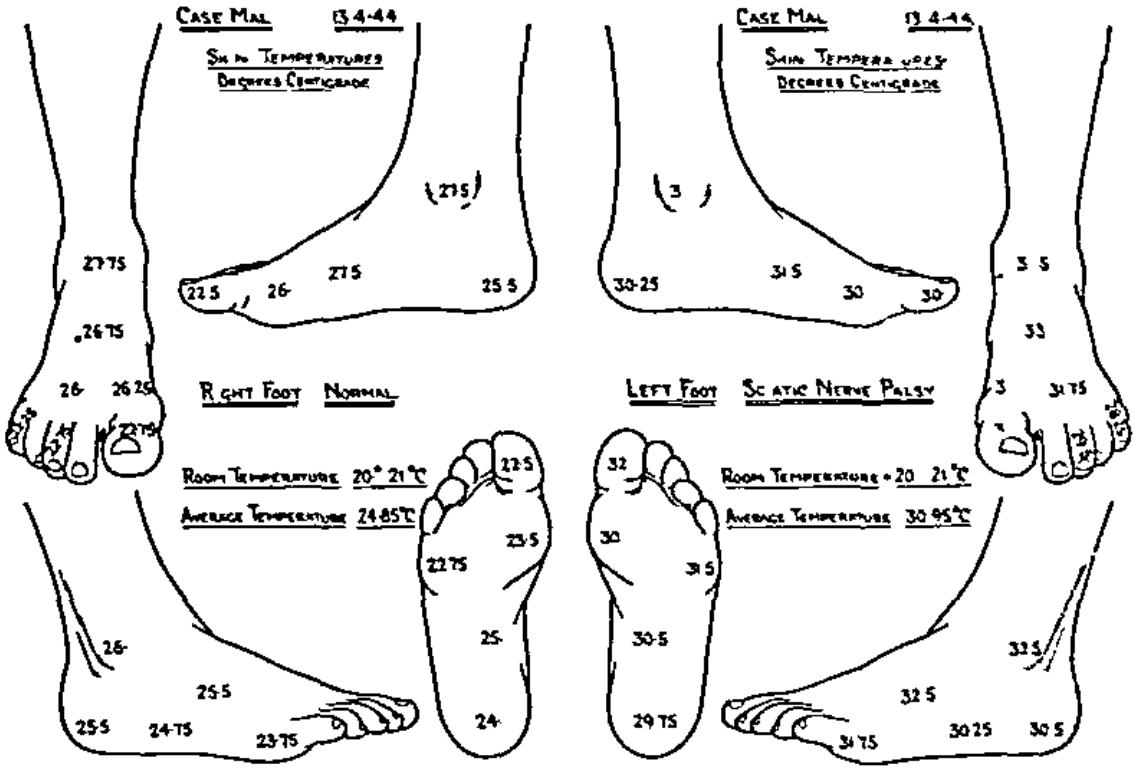

FIG 73
Complete division of left sciatic nerve note higher skin temperature of denervated foot

normal one and this warmth is maintained even after a long period of exposure to room temperature (Fig 73) It has been noted however, that in winter out patients, when reporting frequently arrive with an icy cold foot One very intelligent patient who had had a complete sciatic nerve palsy for 25 years, stated that so long as he took good care never to expose his foot to the cold, it was always warm but that if he allowed it to become cold, it was many hours before it recovered its warmth Division of the external popliteal nerve rarely causes any change in the subjective or objective temperature of the foot After interruption of the internal popliteal or posterior tibial nerve the foot is colder than normal both objectively and subjectively

(2) *Effect of Local Temperature* —The effects of local temperature upon denervated areas in the foot are similar to those in the hand Because of the differences in the innervation of the foot and hand, it is rare to secure complete denervation of the toes unless the sciatic nerve be divided The influence of local temperature upon the normal and the denervated foot is shown in Fig 74 The denervated foot is initially the warmer, but when the feet are cooled, the temperature of the great toe falls progressively towards that of the environment, whereas the normal toe is able to maintain a higher temperature, and between 20 and 30 minutes after exposure to cold, exhibits a characteristic reaction When the feet are removed from the cooling influence the toes warm in a parallel manner towards room temperature, but immersion of the hands in hot water causes a rapid rise in temperature of the normal toe without affecting the denervated toe This demonstrates very clearly how the temperature of the denervated foot depends upon that of its environment

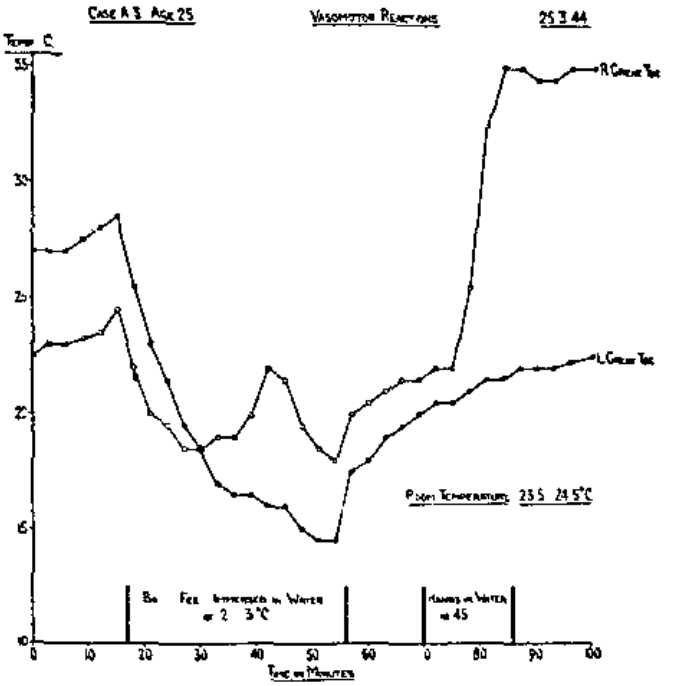

FIG 74
Complete division of left sciatic nerve to show effect of local temperature upon the denervated foot

(3) *Vasomotor Reflexes after Nerve Division* —Complete division of the sciatic nerve invariably abolishes reflex vasomotor activity in the toes The affected foot is usually the warmer and the digits cool slowly towards room temperature, while those of the normal foot exhibit the typical responses (Fig 75) Division of either of the main terminal branches of the sciatic nerve may modify but not abolish reflex vasomotor activity in the toes Vasoconstrictor fibres to the toes are thought to run mainly in the posterior tibial nerve, since procaine block of this nerve results in almost full vasodilatation in the toes Complete division of the posterior tibial nerve alone modifies vasomotor activity in the toes very slightly (Fig 76) When division of the external popliteal nerve produces the classical area of sensory loss confined to the dorsum of the foot, there is no disturbance of reflex vasomotor activity in the toes (Fig 77) In one case division of the external popliteal nerve in the popliteal fossa resulted in complete loss of sensation and vasomotor paralysis in the first three toes (Fig 78) It is probable that this abnormality was a result of a communication in the leg between the internal and external popliteal nerves In the foot the internal and external plantar nerves correspond to the median and ulnar nerves respectively It is, therefore, to be expected that if either of these nerves were divided, a response similar to that from a lesion of the corresponding nerve in the

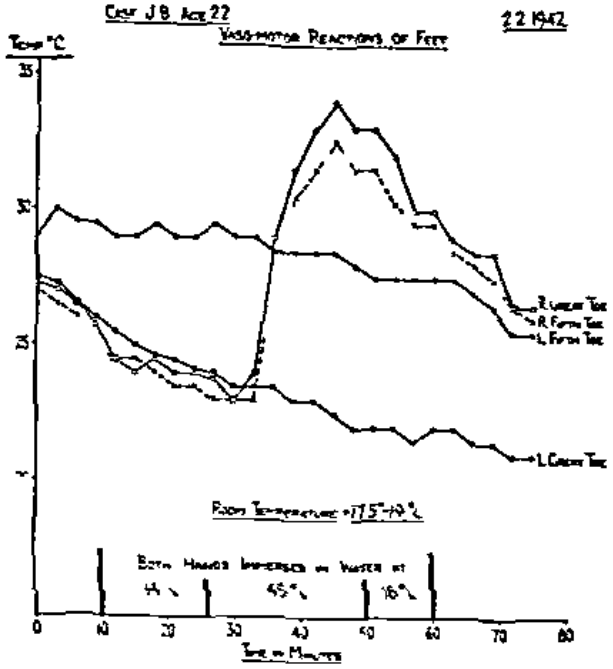

FIG 75
Complete division of left sciatic nerve, note absence of reflex vasomotor response in toes of left foot

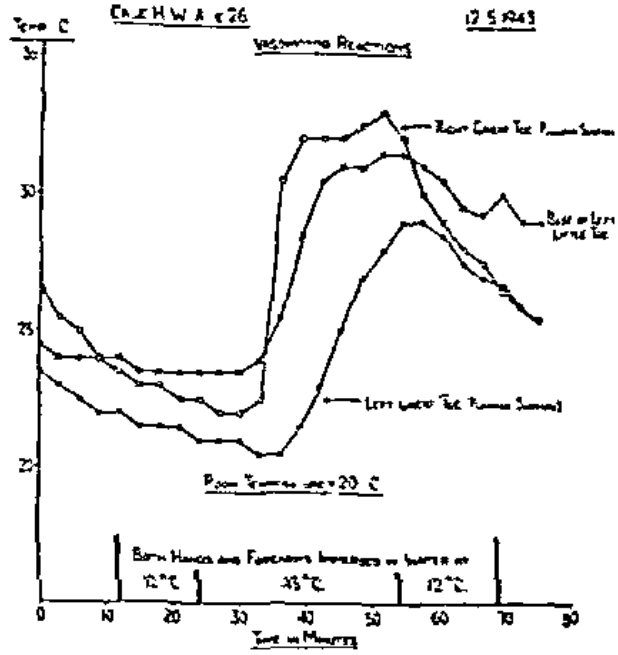

FIG 76
Complete division of left posterior tibial nerve, note difference in the responses of right and left great toes

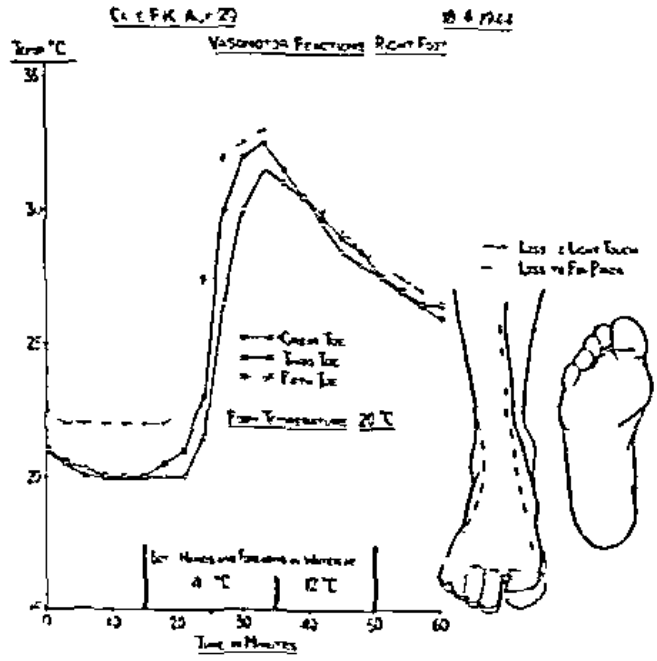

FIG 77
Complete division of right lateral popliteal nerve note area of sensory loss and normal vasomotor response in all toes.

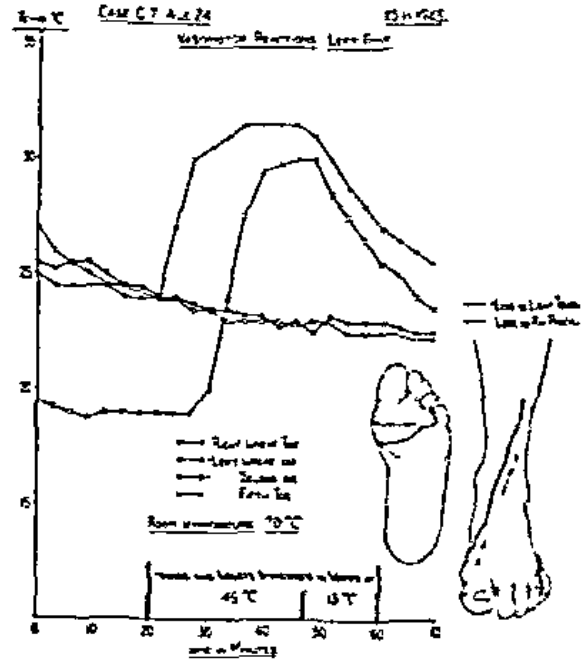

FIG 78
Complete division of left lateral popliteal nerve; note abnormal area of sensory loss extending on to the sole and absence of normal vasomotor response in left great and second toes

hand would be obtained In the present series there has been one case with a lesion of the external plantar division of the posterior tibial The responses in this case are shown in Fig 79 Lesions of the saphenous nerve alone do not affect the vasomotor reflexes in the foot This observation and the absence of vasomotor activity in the foot after sciatic nerve lesions suggest that the saphenous nerve does not carry any vasomotor fibres to the foot Yet in a case where both the saphenous and the posterior tibial nerves were divided, the response in the toes was less than that usually observed after isolated lesions of the posterior tibial (cf Figs 80 and 76) Isolated lesions of the musculo-cutaneous, anterior tibial and sural nerves are not common When they do occur, they are rarely explored and the clinical manifestations are so slight that it is difficult to be certain that complete division has occurred In one patient in whom the musculo-cutaneous nerve was deliberately divided at operation no significant disturbance of reflex vasomotor activity in the toes could be detected

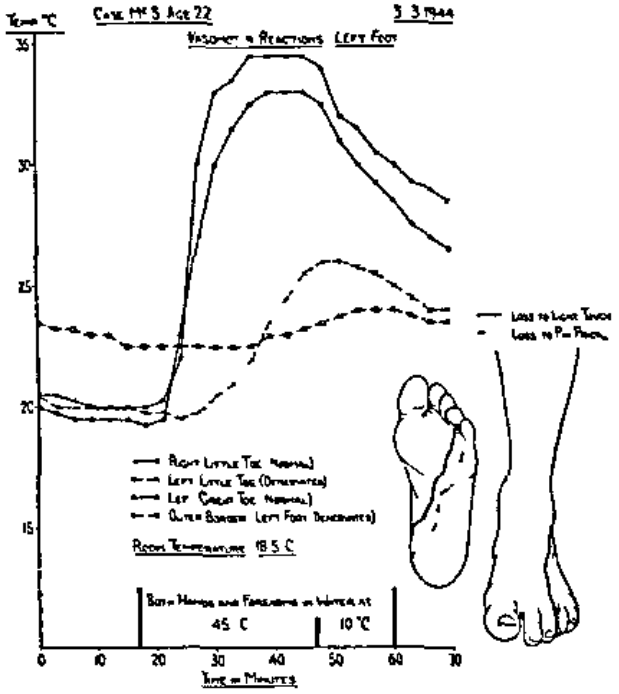

FIG 79
Lesion of left lateral plantar nerve, to show loss of sensation and vasomotor responses of toes

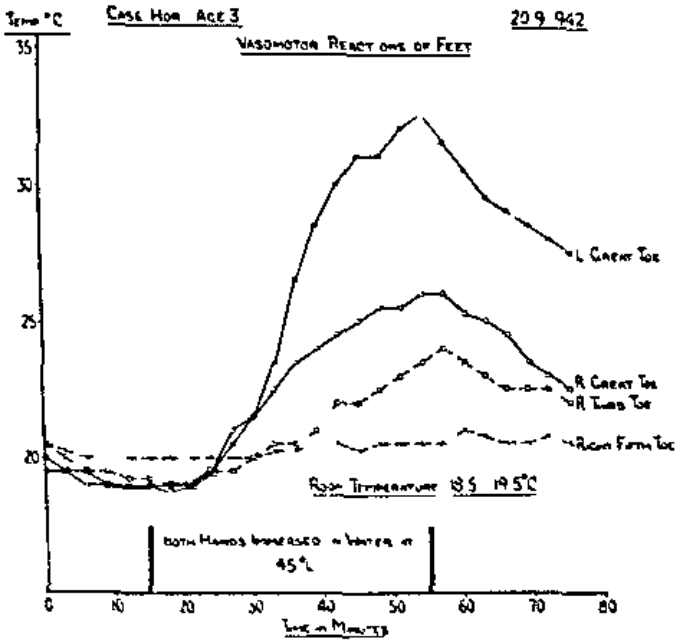

FIG 80
Lesion of right posterior tibial and saphenous nerves, note relatively poor response in all toes of right foot

C Discussion.

The immediate vasomotor effects of nerve division are due to the interruption of vasoconstrictor sympathetic fibres Every peripheral nerve injury, even the Klumpke type of brachial plexus palsy in which the first thoracic root is torn, produces a lesion of which the sympathetic component is essentially post-ganglionic in type In the upper

limb the effect produced is similar to that which follows the operation of stellate ganglionectomy, but is more localised in its distribution The standard sympathectomy for the lower limb is predominantly preganglionic This must be remembered when comparing a sympathectomised foot with the foot after division of the sciatic nerve Initially both sympathectomy, whether preganglionic or postganglionic, and division of a peripheral nerve cause cutaneous vasodilatation

The later effects are more difficult to explain It is known that after about 3 weeks the cutaneous blood vessels of a sympathectomised limb regain a certain amount of control It need scarcely be stated that such an early return of control is not due to nerve regeneration Trotter and Davies (1909) observed that after nerve division the vasomotor changes were the first to disappear They did not, however, as has been suggested in a recent leading article,[1] ascribe this to nerve regeneration Denervated blood vessels will not respond reflexly on the application of cold or warmth to other parts of the body, but they will contract and relax in response to local changes in temperature (Lewis and Landis, 1930) The blood flow to a sympathectomised hand differs from normal in that it varies with the metabolic needs of the tissues and not with the body temperature (Freeman 1935) The close relationship between the temperature of a denervated area and that of its environment has already been stressed A reduced blood flow from the reduction of metabolism which must take place in a denervated area, and the direct effect of low environmental temperatures on the denervated cutaneous blood vessels, are probably the chief local factors concerned in the development of the cold phase If the metabolic needs of a denervated area are raised, then an increase in local blood flow will result After division of the median nerve an index finger which is the site of a superficial infection becomes the warmest digit of the hand Doupe and Cullen (1943) studied the problem of inflammation and ulceration in denervated areas and found that infection raises local temperature in the normal manner These findings are at variance with those of Breslauer (1919) already quoted (p 90) It is apparent that some cause other than a defective circulation must be sought to explain the slow healing of ulcers in

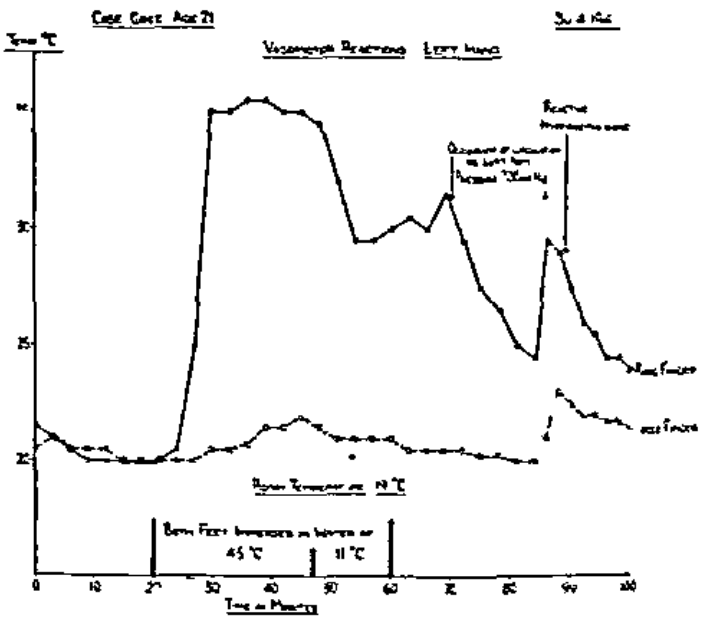

FIG 81

Complete division of left median nerve, note absence of reflex vasodilatation in index finger but rise in temperature during reactive hyperaemia

[1] *Brit Med J* May 15th 1943

denervated areas Repeated minor traumata to the already injured insensitive area, and local oedema, particularly in the lower limb, are probably sufficient to account for the apparent delay in healing

Further evidence that the blood supply to denervated areas is regulated by, and adequate for, local tissue metabolism, is provided by the phenomenon of reactive hyperaemia After division of either the median or ulnar nerve, provided the temperature of normal and denervated areas of the hand is similar, the intensity of the reactive hyperaemia which follows a period of circulatory arrest is uniform throughout Furthermore, a digit which exhibits little or no rise in temperature after reflex vasodilatation will show an appreciable rise during the period of reactive hyperaemia (Fig 81) The stimulus for vasodilatation in denervated areas is provided by locally produced metabolites, and it is of interest that a denervated digit will show vasodilatation in response to an injection of histamine (Lewis and Pickering, 1936)

The calibre of denervated blood vessels is also controlled by substances circulating in the blood stream, of which adrenalin is the most important The return of vascular tone after sympathectomy is attributed to a raised responsiveness to humoral stimuli on the part of the cutaneous blood vessels (Grant, 1935 , le Compte, 1941) White and Smithwick (1942) have shown that, following postganglionic sympathectomy, the cutaneous vessels in a limb are hypersensitive to physiological concentrations of circulating adrenalin, and Atlas (1938 and 1941) has suggested that a similar mechanism is the cause of the nutritional lesions in nerve injuries Doupe (1943b) has shown that the blood vessels in denervated digits exhibit a lowered threshold and a prolonged response to adrenalin, whereas after preganglionic sympathectomy they show a lowered threshold only The sensitivity of denervated vessels to adrenalin is known to be at its maximum about the 21st day after sympathectomy, and this period would coincide with the accepted interval after nerve division before the onset of the 'cold phase" The fall in skin temperature produced by physiological concentrations of adrenalin in both Atlas's and White's experiments is not more than 3-4°C , and it is difficult to believe that such a mechanism could be responsible for the sudden drop from temperatures of 32 35°C to 19-20°C , or even lower, that takes place at the critical period Doupe (1943b), however, has shown that adrenalin can be liberated in the body in amounts which would almost certainly be sufficient to initiate and maintain vasoconstriction in a denervated digit It is also of importance to note that Grant and Pearson (1938) and Fatherree *et al* (1940) have cast considerable doubt on the hypothesis that circulating adrenalin is the factor responsible for the return of vascular tone after sympathectomy

The difference between a denervated cutaneous area and an area of skin after postganglionic sympathectomy is that the former has lost its afferent nerve supply Sir Thomas Lewis (1936) believes that this is the important factor in the development of the cold phase It has been shown both by Lewis (*loc cit*) and others (Doupe, 1943c) that the presence of afferent fibres is essential for axonal vasodilatation Axonal vasodilatation, occurring as it does in response to minor traumata of all forms, is undoubtedly an important contributory factor in the maintenance of the temperature and nutrition of normal skin Axonal vasodilatation can still be

obtained immediately after peripheral nerve section, but disappears after the sensory fibres have had time to degenerate The interval before the nerves degenerate accounts for the initial warm phase *In support of this hypothesis is the observation* that denervated digits do not regain their normal warmth until the sensory fibres have regenerated (p 119)

The intact innervation of the rest of the limb may be considered as a further factor in the development of the cold phase Although the results of stellate ganglionectomy are not good, there is no doubt that the operation results in a hand which remains warm for a period longer than 3 weeks In the present study it has been noted that an extremity which is almost completely denervated (a hand after a complete tear of the brachial plexus, or a foot after complete division of the sciatic nerve) tends to remain warm The effect of cold is to cause peripheral neurogenic vasoconstriction After nerve division this will still occur in the normally innervated portions of a limb, and a reduction in total blood flow will result If it be assumed that the denervated area was initially warm, then the reduction in blood flow and the direct effect of cold upon the cutaneous vessels will cause it to cool A very slight rise in temperature or an increase in metabolism may be sufficient to warm the body and release the neurogenic vasoconstriction The denervated portion will remain cold because of the direct effect of the low environmental temperature and will warm gradually only as blood seeps into it from the adjacent normal tissues If measures are taken to protect the denervated area from the direct effects of cold, then it does not become cold This is one of the reasons why the denervated foot, which is normally well protected, is seldom found to be in the cold phase whereas if the patient does not wear a glove, a denervated area in the hand may become very cold

These four factors—lowered local metabolism, sensitisation of denervated blood vessels to circulating adrenalin, loss of afferent nerve supply and the integrity of the innervation to the rest of the limb—are probably sufficient to account for the late vasomotor changes in cases of nerve division The possibility that other factors may also be at work cannot be entirely excluded Apart from their important function as the mediators of axonal vasodilatation, the fibres of the posterior root system may have some influence upon the temperature of the limb Zuckermann and Ruch (1934) showed experimentally that there was a difference between the vasomotor state of a completely denervated monkey's lower limb and a limb which is connected to the spinal cord by the posterior roots only The former is colder than normal and cools to a very low temperature on exposure to cold, whereas the latter is warmer and does not cool so readily as a normal limb This was confirmed in man by Lewis and Pickering (1936), who demonstrated that the sympathectomised lower limbs in cases of anterior poliomyelitis tend to remain warm In the upper limb it has recently been shown that, if the anterior roots from C5 to T2 are divided, the vasomotor responses in the hand may not be significantly altered (Learmonth and Richards 1943)

The possibility that following nerve injuries changes take place in the peripheral blood vessels still requires further investigation Stopford (1918) described a case in which definite intimal thickening of the peripheral arteries followed an injury of the sciatic nerve Lewis and Pickering (1936) showed that, compared with the normal,

pulsation in the vessels of a denervated digit was only slightly reduced in volume Philippides (1942) has stated that the fall in temperature in denervated areas which takes place after the first 14 days is due to changes in the blood vessels, and that narrowing of these has been demonstrated histologically Unfortunately, he does not state to which vessels these observations apply In the arteries of a leg amputated 25 years after division of the sciatic nerve, Blackwood (1944) was unable to find any abnormal change

The nutritional disturbances observed in denervated digits, atrophy of the pulp, loss of skin creases, irregularities in nail growth, etc , are the result of a vicious cycle in which disuse, lowered metabolism and the direct vasoconstrictor effect of local cold all play a part Their occurrence is very variable, and even in long-standing complete lesions they may be almost absent if the patient makes good use of the injured limb As Lewis and Pickering (1936) have shown, such changes are not specific to cases of nerve division, but may occur as a result of any condition which causes immobility and disuse of a digit

The Reflex Responses—The observations on reflex vasomotor activity were carried out in order to determine the area over which nervous regulation of vasomotor activity is disturbed following complete division of a peripheral nerve It has been found that this area is never larger than that of the cutaneous analgesia, and is usually smaller Thus in an ulnar nerve lesion, although at rest the whole of the affected hand may be more cyanosed and colder than normally, reflex vasomotor activity is found to be quite normal in the median and radial territories This is to be expected of the peripheral nerves, because it is very likely that they distribute their vasomotor fibres with sensory fibres, but it is a little surprising in lesions of the brachial plexus All the roots of the plexus receive postganglionic sympathetic fibres, and the first thoracic root is particularly well supplied (Kuntz, 1934) Yet it is found that interruption of T1 produces vasomotor effects localised to the little finger, and interruption of C5 and C6 little if any change in the digits This is yet *another indication of the diffuse and overlapping nature of the peripheral sympathetic* outflow in man

In studying the results of vasomotor responses to decide the extent of the distribution of vasomotor fibres from any particular nerve, it is important to realise that the abrupt rise of temperature is dependent not upon the minute cutaneous vessels, but on the arteriovenous anastomoses and larger vessels in the deeper layers of the skin and in the subcutaneous tissue Woollard and Phillips (1932) stated that the peripheral distribution of the sympathetic vasomotor fibres corresponds to that of the sensory fibres The evidence on which this opinion was based was obtained by blocking peripheral nerves with local anaesthetic, and studying the vasomotor changes which followed The cutaneous hyperaemia which follows the blocking of such nerves as the median and the ulnar undoubtedly corresponds very accurately with the area of cutaneous analgesia As Telford and Stopford (1933) point out, this can be accepted as evidence only that the small superficial blood vessels of an area of skin receive their vasoconstrictor fibres from the same nerve as supplies it with its sensory fibres Cutaneous hyperaemia is accompanied by very

little rise in surface temperature (p 54) In Woollard and Phillips's experiments, the rise in skin temperature was never very marked (only 1-2 C), and it is doubtful if they succeeded in producing a complete vasomotor paralysis in any of the digits Highet (1942) has applied the procedure of procaine nerve block in the investigation of peripheral nerve injuries, and as a result of his observations states that the peripheral distribution of vasomotor fibres from the median, ulnar and radial nerves corresponds to that of the unmyelinated fibres subserving pain and sweating. Philippides (1942) has blocked the postganglionic sympathetic fibres to the arm by injecting the stellate ganglion with procaine He believes that this is a valuable diagnostic procedure since the responses so obtained are absolutely clear cut In cases of complete nerve division, a rise in temperature does not take place in the autonomous territory of the divided nerve If any rise in temperature does take place, it is an indication that the nerve lesion is incomplete and will probably recover without operation

The present method was adopted as being simpler and less troublesome to the patient than that of injecting local anaesthetic It was also hoped that, since this method depends upon an active reflex process occurring in the body and is thus more physiological than the method of nerve blocking it would be more likely to give a reliable indication of the effective distribution of vasomotor nerve fibres

The results from investigation of the ring finger show that a considerable overlap of vasomotor fibres from one nerve territory to another does take place, for interruption of either the median or ulnar nerve alone fails to modify significantly the vascular responses of this digit Similarly, in the thumb a considerable overlap in the vasomotor fibres from the median and radial nerves must be present (The evidence at present available suggests that these are the only two nerves concerned in the innervation of the blood vessels of the thumb) The slight and delayed rises in temperature seen in completely denervated digits which are adjacent to normally innervated areas (that is the little finger in an ulnar palsy and the middle finger in a median palsy), suggest that the overlap may be even more extensive Duthie and Mackay (1940) recorded a similar rise in temperature in the little finger in a case of ulnar palsy, and believed that the vasodilatation was the result either of inhibition of the action of vasoconstrictor fibres which reached the little finger via the median nerve, or of the action of vasodilator fibres which were not interrupted by division of the ulnar nerve

It is doubtful if these incomplete responses can be accepted as evidence of *reflex* vasomotor activity The increase in blood flow to the hand when reflex vasodilatation is at its height is very great indeed, Brown and Allen (1941) have recorded increases as high as 200 per cent This must result in a greatly increased flow of blood through the palmar arches metacarpal and digital arteries It is difficult to believe that the nerve supply of these deeper and larger vessels corresponds exactly to cutaneous sensory territories and they are probably considerably dilated even in the presence of a nerve lesion The dilatation of these vessels must result in a considerable increase in the temperature and metabolism of the adjacent tissue As already pointed out (p 104) denervated blood vessels are susceptible to local temperature

changes and the local metabolic needs of the tissues The vessels supplying a digit adjacent to a normal area will therefore be affected secondarily by the reflex vasodilatation in that area, and will tend to dilate The delay before any response is noted in a completely denervated digit is thus explained , and the gradual nature of the rise in temperature can also be explained on this basis It is the result of a vascular dilatation which is dependent upon the accumulation of local metabolites in the tissues Since the initial blood flow to a denervated digit is low, such substances will accumulate and be destroyed or removed slowly compared with the labile chemical mediators responsible for activity at the sympathetic nerve endings in a normal digit Further, the local accumulation of these metabolites will tend to *cause the dilatation to persist even after the stimulus for reflex vasodilatation has* been removed This is well illustrated by the response of the little finger in Fig 64, where the temperature remains elevated while that in the other digits is falling rapidly

In considering the results produced by reflex vasodilatation, it is maintained that only an abrupt rise in temperature of at least 5°C is definite evidence of reflex vasomotor activity in a digit , if this be accepted, the observation of Lewis and Pickering (1936) that denervated digits do not respond to a rise in body temperature is confirmed The slow and incomplete responses seen in such digits are the result of the action of chemical substances produced secondarily and acting locally This is a further indication of the way in which the integrity of the nerve supply to the blood vessels of the rest of the limb influences the vasomotor state of a denervated area Since sympathectomy destroys all the vasoconstrictor nerves to a limb, this factor is not operative in a sympathectomised limb

These arguments, which have been supported by referring to results obtained in the hand, apply equally to the foot The innervation of the foot is such that it is rare for complete denervation of a single toe to occur The results shown in Figs 78 and 79, however, make it clear that denervated toes respond to reflex vasodilatation in a similar manner to denervated fingers A partially denervated toe, like a partially denervated finger, may show an almost normal response It may be concluded that after complete nerve division the physiological processes underlying the vasomotor disorders in the upper and lower limbs are fundamentally similar in the denervated area local factors assume control of the circulation These views are in agreement with those recently put forward by Doupe (1943a) as the result of a series of similar observations upon the circulation in denervated digits

INCOMPLETE NERVE LESIONS

Incomplete lesions of peripheral nerves may result from any form of trauma which is insufficient to cause complete interruption of the nerve The effect of the trauma upon the constituent fibres of the nerve will depend upon the relative number of the different types of fibre, their arrangement within the nerve and their vulnerability In respect of vasomotor fibres, anatomical information regarding the first and second of these important points is lacking It is known that certain nerves (median, posterior tibial) contain a higher proportion of vasomotor fibres than others (radial, external popliteal), but the relative number of vasomotor fibres in the main

peripheral nerves of man has not been ascertained In the dog, Nevin (1930) found that the majority of unmyelinated fibres in the peripheral nerves were of sympathetic origin The proportion of unmyelinated to myelinated fibres in the peripheral nerves in man varies from 5 1 in purely cutaneous nerves to 0 7 1 in motor nerves (Ranson *et al*, 1935) It is certain that in man not all unmyelinated fibres are of sympathetic origin, even if it were so, it would be impossible to decide how many of such fibres subserved vasomotor activity, and how many the other sympathetic functions The arrangement of vasomotor fibres within the nerve is also unknown Modern teaching (Seddon, 1943) is opposed to the hypothesis of a relatively constant intraneural topography, and it is probable that sympathetic fibres are widely scattered throughout the nerve More is known concerning the vulnerability of vasomotor fibres There is general agreement that the small unmyelinated fibres, to which group the vasomotor fibres belong are the least susceptible to the effects of pressure or ischaemia upon a nerve (Gasser, 1935, Lewis and Pochin, 1937, Wortis *et al*, 1942) Their vulnerability to other forms of trauma, with the exception of cold (Waller, 1862, Bickford, 1939) and cocaine (Gasser and Erlanger, 1929) has not been so clearly defined

After an incomplete lesion of a peripheral nerve, three types of axons may be present within the nerve (1) axons that have been completely interrupted, (2) axons that are in anatomical continuity but have impaired function, (3) normal axons to these after a period may be added (4) regenerating axons Axons carrying both afferent and efferent impulses may be affected by any or all of these processes It follows that the theoretically possible clinical manifestations of an incomplete peripheral nerve lesion are innumerable In practice a fairly restricted variety of disturbances are seen With regard to vasomotor functions, three possibilities may be considered —

(*a*) *Vasomotor fibres alone might be affected* —This type of lesion may be produced experimentally by weak solutions of cocaine, but is not seen in clinical practice It is theoretically possible, however, to have an injury of the sympathetic chain which might disturb autonomic functions alone

(*b*) *Vasomotor fibres might escape and motor and/or sensory fibres be affected* — From observations on complete nerve lesions, it is apparent that in the majority of cases analgesia in an area of skin is accompanied by vasomotor paralysis in that area This has been found to be the case in the majority of incomplete lesions A dissociation between motor functions on the one hand and sensory and vasomotor functions on the other, is not uncommonly encountered As might be expected from the experimental work, this type of lesion is seen most frequently as the result of external pressure upon a nerve

Certain peripheral nerves are more subject to the effects of pressure than others, the radial and ulnar nerves in the upper limb and the external popliteal in the lower limb are typical examples Acute pressure upon a nerve produces a characteristic type of lesion motor paralysis without loss of sensation is the presenting symptom and recovery is rapid and complete Even in the most severely affected fibres the lesion is an interference with function (neurapraxia) The common lesion of this

type is the " drunkard's palsy " of the radial nerve Apart from coldness and blueness of the hand attributable to dependency and disuse, this type of palsy produces no vasomotor disturbance Since complete division of the radial nerve scarcely affects the vasomotor state of the hand, this cannot be accepted as evidence that in acute pressure lesions vasomotor fibres escape damage Seddon (1943) has demonstrated that in this type of lesion the large medullated fibres subserving motor activity and proprioceptive sensation suffer most severely, and that pain and sudomotor fibres are relatively slightly affected It may be assumed that vasomotor fibres also tend to escape

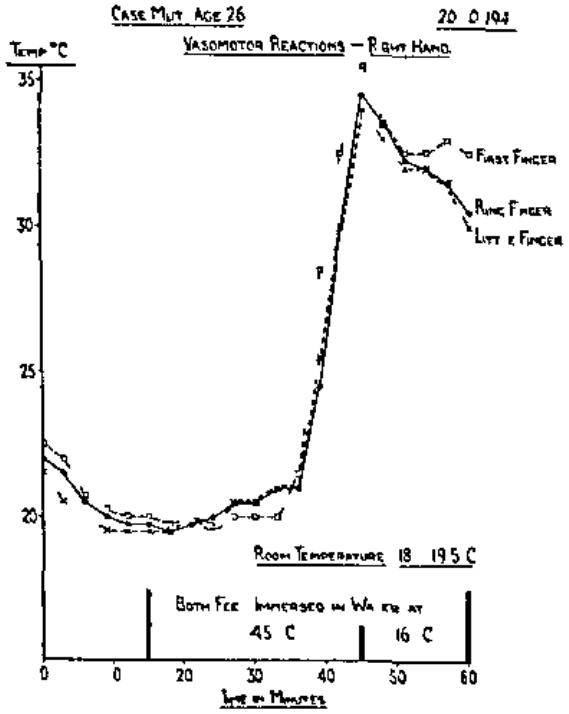

FIG 82
Right tardy ulnar palsy note normal response in little and ring fingers

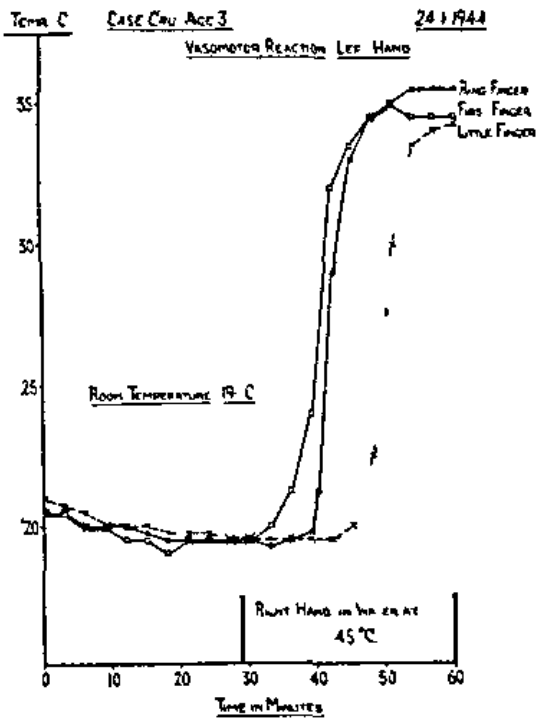

FIG 83
Case CRU Left ulnar lesion , normal vasomotor response in little finger

A more severe type of lesion results from prolonged pressure upon a nerve , a certain number of fibres may be interrupted with resultant neuroma formation An excellent example is the tardy ulnar palsy[1] that develops after malunion of a supra-condylar fracture of the humerus, or as a result of a congenital cubitus valgus with a shallow ulnar groove and recurrent dislocation of the nerve In this type of lesion the manifestations are the gradual and progressive onset of motor paralysis with subjective sensory disorders , except in long-standing cases objective loss of sensation is slight Almost without exception patients complain that the affected hand is colder and more sensitive to cold than the normal hand Objective confirmation of this is usually obtained , the whole affected hand feels cooler than its fellow and is more cyanosed Reflex vasomotor activity in the digits is usually normal (Fig 82)

A similar dissociation is sometimes observed as a result of a missile wound Case CRU (Fig 83) This patient sustained a gunshot wound of the left wrist

[1] Factors other than pressure, *e g* stretching are probably concerned in the production of this lesion

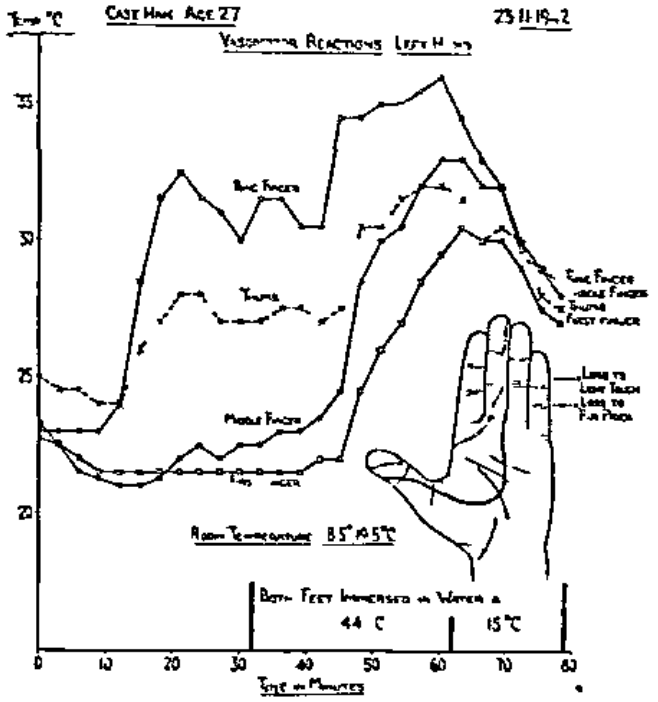

FIG 84
Case HAN Left median nerve lesion pre-operative to show loss of sensation and vasomotor reactions

of the left median nerve above the elbow responses of the digits before operation are shown in Fig 84 At operation, the nerve was completely divided and suture performed After operation the sensory picture had not altered, but the vasomotor response in the index finger was abolished (Fig 85)

(c) *There may be evidence of perversion of function of vasomotor fibres with or without evidence of damage to motor and or sensory fibres* —A lesion which interferes with the function of nerve fibres may have two results First it may interrupt the passage of normal centrifugally directed impulses Vasoconstrictor fibres are constantly carrying impulses responsible for the maintenance

involving the ulnar nerve Complete paralysis of the interossei and hypothenar muscles resulted, but there was negligible sensory loss and no vasomotor disturbance Procaine block of the median nerve (Highet, 1942) demonstrated that the dissociated paralysis was not the result of an anomalous innervation of the hand The ulnar nerve was later explored, a lesion resected and suture performed After operation there was complete loss of sensation and vasomotor paralysis in the little finger

Dissociation between sensation and vasomotor activity is rare In the present series only one case of this nature has been observed Case HAN This patient had an incomplete division The loss of sensation and vasomotor

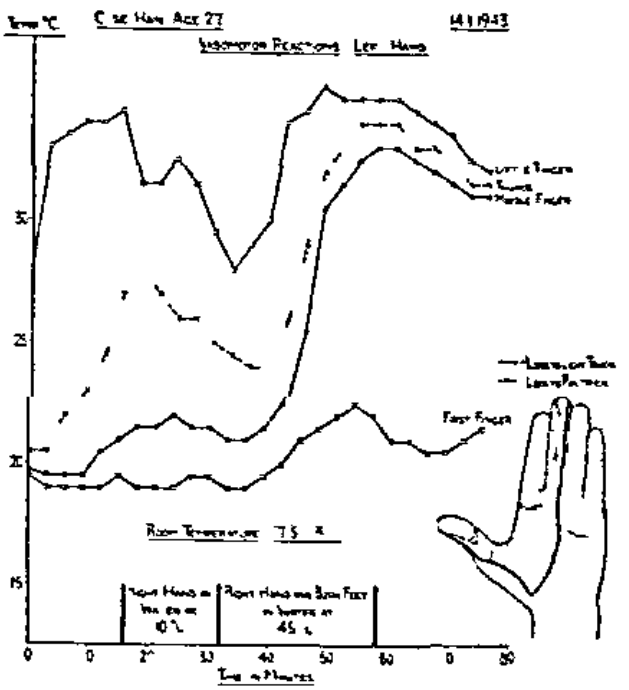

FIG 85
Case HAN Post-operative for comparison with Fig 84

of vasoconstrictor tone Incomplete nerve division may reduce the total number of such impulses in two ways (1) by complete interruption of a certain number of vasomotor fibres and sparing of others, and (2) by interfering with conduction in all fibres The result in either case will be a reduction in peripheral vasoconstrictor tone Secondly, the lesion may be responsible for an abnormal discharge of impulses Adrian (1932) has shown that injury to a nerve fibre causes a periodic discharge of impulses along that fibre Abnormal afferent impulses arising at the site of a lesion are thought

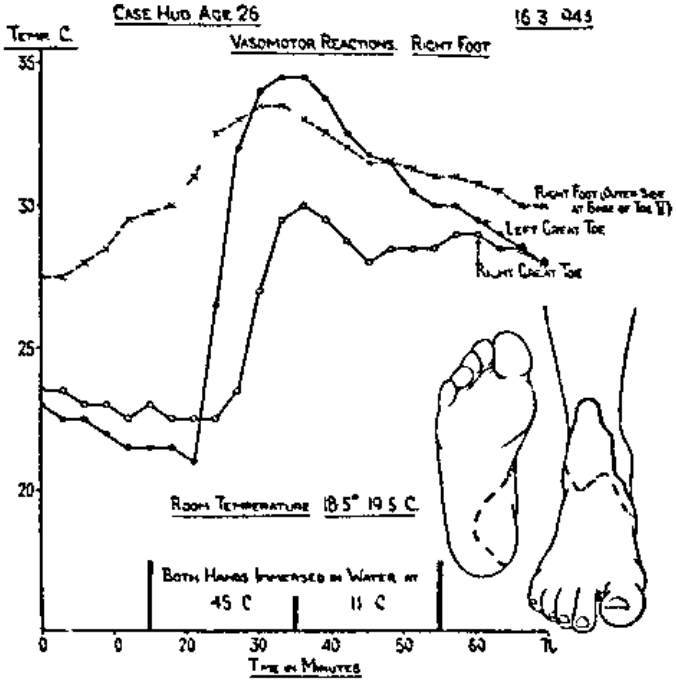

FIG 86

Nerve lesion following closed fracture of both bones of the leg to show loss of sensation and vasomotor reactions

to be responsible for many of the painful syndromes which may follow nerve injury Abnormal efferent impulses may therefore be responsible for vasomotor disorders Centrifugally directed impulses in vasoconstrictor fibres would be responsible for abnormal vasoconstriction Impulses passing along sympathetic vasodilator fibres or along the fibres responsible for axonal vasodilatation, would cause peripheral vasodilatation

Wilkins and Kolb (1941) found that a decrease in vasoconstrictor tone was the predominant vasomotor disorder in cases of polyneuritis Vasoconstrictor tone is greater in the lower limbs, and injury of the sciatic nerve and its branches not uncommonly produces a lesion with this type of vasomotor abnormality Nerve palsies following fracture of the bones of the leg are frequently incomplete The vasomotor responses in a case of this nature are shown in Fig 86 There is a general lowering of vasoconstrictor tone in the right foot, and a diminished reflex response to immersion of the upper limbs in hot and cold water Nerve ischaemia has been

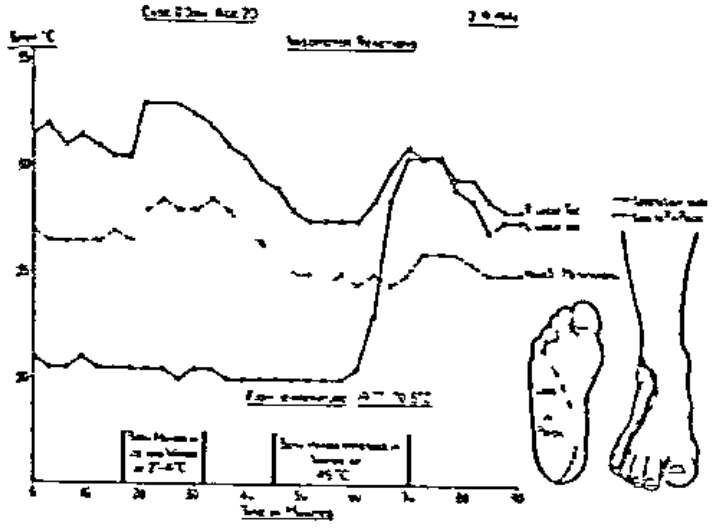

FIG 87

Case OD Haemorrhage into right sciatic nerve, loss of sensation and vasomotor reactions five months after injury

suggested as a possible aetiological factor in lesions of this type (Parkes, 1944) The relative sparing of vasomotor fibres is in support of this hypothesis In another case (Figs 87, 88 and 89), a gunshot wound of the thigh caused a haemorrhage into the intact sheath of the sciatic nerve In the period from 5 to 9 months after injury, the vasomotor responses illustrate the gradual recovery of normal vasoconstrictor tone and normal reflex vasomotor activity

Abnormal vasoconstriction after a nerve injury is exceedingly difficult to demonstrate The habitual coldness of denervated areas is not the result of neurogenic vasoconstriction The presence of coldness, cyanosis and excess sweating in an incompletely denervated area, and the abolition of these symptoms by procaine block of the affected nerve at or distal to the site of the lesion, would be the only reliable evidence Cases of this nature have been described by Leriche (1939), but have not been observed in the present series

Consideration of peripheral vasodilatation resulting from an incomplete nerve injury leads inevitably to the problem of causalgia This condition, which was named and described fully for the first time by Weir Mitchell and his colleagues (1864) has never been adequately defined. Carter (1922) refers to it as a painful vasomotor neurosis due to irritation of a mixed nerve " It is a condition in which severe *spontaneous* pain is experienced in the cutaneous territory of an injured nerve (usually the sciatic or median) associated with profound vasomotor disturbances, and, if the

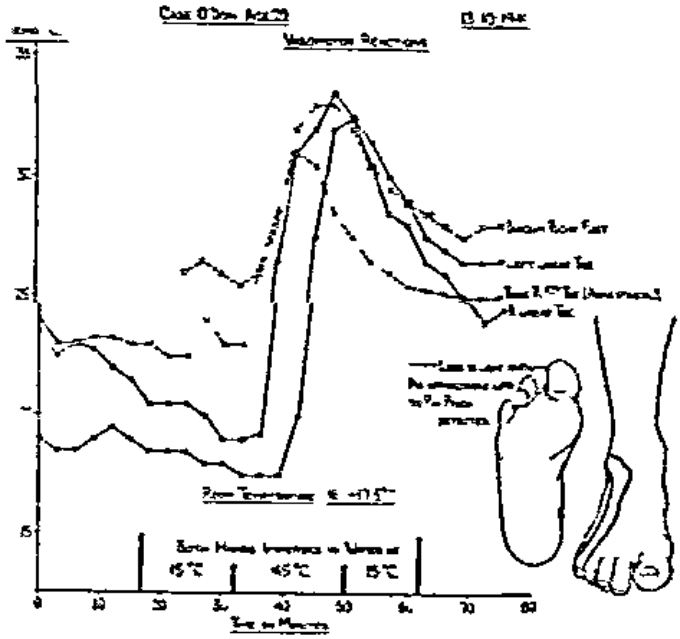

FIG 88

Case OD At six months.

condition has been present for any length of time, with a general hypersensitiveness of the nervous system The majority of the descriptions of the syndrome (*e g* Carter, 1922, Lewis, 1942, de Takats 1943 and 1945) stress vasodilatation as the vasomotor disturbance, Stopford (1918) was so impressed by the vasodilatation that he suggested "thermalgia" as an alternative name for the condition Leriche (1939), however, speaks of "causalgias of vasoconstriction and causalgias of vasodilatation" In general, objective signs of interference with nerve function other than the vasomotor upset are slight It is therefore generally believed that the vasodilatation of causalgia is an irritative and not a paralytic phenomenon In this war, cases of causalgia have been rare In the present series only 3 cases (1 median, 2 sciatic) have satisfied the criteria for causalgic pain (M R C Report, 1920) of these, only one has been suitable for vasomotor studies This was a case in which the internal popliteal nerve was affected The patient complained of the persistent burning pain in the left foot He stated that the affected foot was always objectively hot, and he kept it cool and moist by the application of a wet cloth Many vasomotor tests were carried out on this patient It was found that after he had been out of doors the affected foot might be cool, but that shortly after coming into a cool or warm room and having thermocouples attached to the toes, the foot warmed spontaneously (Fig 90) There was, however, a definite indication of some reflex vasomotor activity in the toes of the affected foot These findings do not differ from those obtained in other patients with

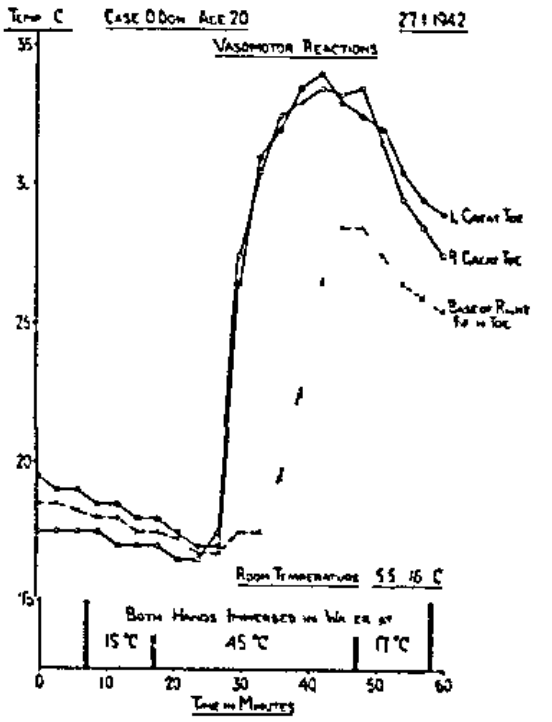

Fig 89
Case OD At nine months vasomotor reactions now almost normal, no sensory loss

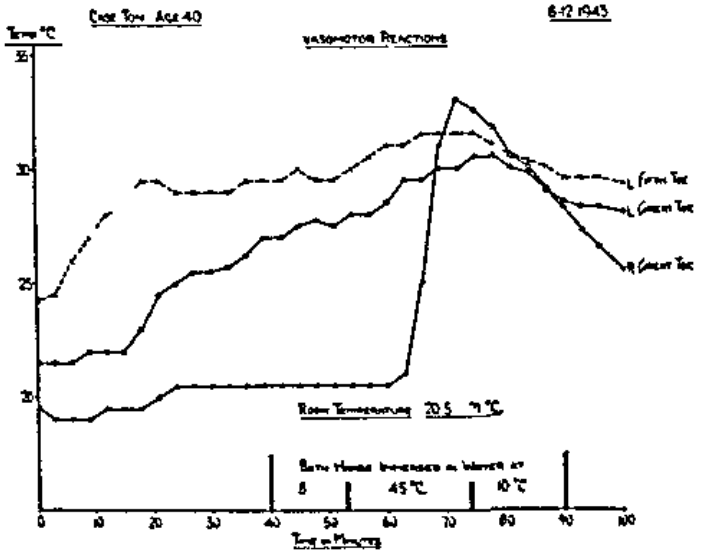

Fig 90
Left sciatic causalgia, note spontaneous rise in temperature in toes of left foot

incomplete lesions of the sciatic nerve who did not have causalgia In the case where the median nerve was affected, the brachial artery had been ligated elsewhere before the patient came under observation This had not relieved the pain, but, possibly as a result of this procedure, the affected hand was usually the cooler In many cases of nerve injury all the classical objective features of the causalgic syndrome may be present but the essential burning pain is absent Similar results have recently been reported by Doupe *et al* (1944) In cases of causalgia they found that the temperature of the affected digits was frequently higher than that of the normal contra lateral digits This was not invariable, however, and in the majority of their cases reflex vasomotor activity in response to warming and cooling of the indifferent limbs was preserved These rather limited observations suggest that an irritative vasodilatation is not an essential feature of causalgia This opinion is supported by Livingston (1943) who states " In relatively few instances of what I would call causalgia, is a local rise in temperature seen as a persistent feature More often, when it does occur, it is transient and is followed by a fall in temperature so that the involved part is colder than normal "

Homans (1940) and Livingston (1943) have described a condition to which they have given the name minor causalgia " This condition is usually a sequel to a minor injury and frequently follows the amputation of a finger After the amputation the patient complains of constant pain in the amputation stump which is exquisitely tender to the touch The stump and surrounding area, sometimes the whole hand, is cold, cyanosed and often sweats excessively Exposure to cold aggravates the pain moderate warmth relieves it The following case appears to be a typical example —

Private JA aged 30, sustained an accidental bullet wound of the left hand on 20 5 40 The wound healed without complications, but from the time of the injury he was conscious of numbness of the index finger In August, 1940, he complained of a dull throbbing miserable ' pain in the radial side of the palm at the site of the scar This pain was most severe when the hand was exposed to cold, and was accompanied by a circulatory disturbance in the hand the whole hand would become blue and cold the index purple and " little red streaks " would appear on the fingers The pain was relieved and the hand restored to its normal appearance by warmth On examination at another hospital in January, 1941, there was found to be anaesthesia of the palmar surface of the index and analgesia of the distal phalanges. Flexion of the digit was impaired, due to damage to the flexor tendons in the palm There was a local trigger spot and a small palpable neuroma on the radial side of the index pressure upon this caused severe pain The index finger was amputated and this afforded relief for 5 months In September, 1941, he was re admitted to hospital with a recurrence of his previous symptoms He was found to have a tender amputation scar and a palpable neuroma over the head of the second metacarpal which had not been removed at the time of the amputation Procaine infiltration of the scar gave relief from pain and caused the hand to become warm Reflex vasodilatation induced by heating the right hand was also effective in relieving pain in the left hand A second operation was performed , the distal two-thirds of

the metacarpal and a neuroma on the digital nerve to the radial side of the index were removed This gave immediate and complete relief from pain

Cases of this nature are not uncommon even in civilian practice, and are not found exclusively after nerve injuries That there is some connexion between the vasomotor disorders seen in these cases and those that follow incomplete lesions of peripheral nerves cannot be doubted, and this, therefore, appears to be the correct place to consider the problem In many of the cases a functional element may be added to the organic disorder before the patient comes under observation Pain and the fear of injury to the tender area result in immobility and disuse, both of which contribute to the coldness and cyanosis of the hand This is insufficient to account for the occurrence of spasmodic attacks of vasoconstriction which are associated with exacerbations of pain It is suggested that the vasoconstrictive phenomena are the result of a spinal reflex Abnormal afferent impulses arising either from nerve endings involved in scar tissue (Livingston, 1943), or from receptors in the blood vessels (Homans, 1940), reach the spinal cord via the posterior roots and provoke a discharge of impulses along sympathetic fibres This hypothesis is supported by the immediate relief of pain and recovery of warmth which is brought about by procaine block of the " trigger " area

Knowledge of the disordered physiology which underlies these painful post-traumatic syndromes is far from complete It appears, however, that the vasomotor disorders which accompany them may be explained upon sound physiological concepts All the vascular phenomena which have been described in the present section appear to be explicable upon the basis of interference with sympathetic vasoconstrictor fibres, and the hope that fresh evidence would be forthcoming in favour of the hypothesis that there are vasodilator fibres in the peripheral nervous system of man has not been realised

RECOVERING NERVE *LESIONS*

A permanently denervated area of skin remains in the cold phase and fails to show reflex vasomotor activity Recovery of vasomotor activity may therefore be assumed to indicate reinnervation of the area by vasomotor fibres As yet the opportunity of studying cases in the recovery phase has been

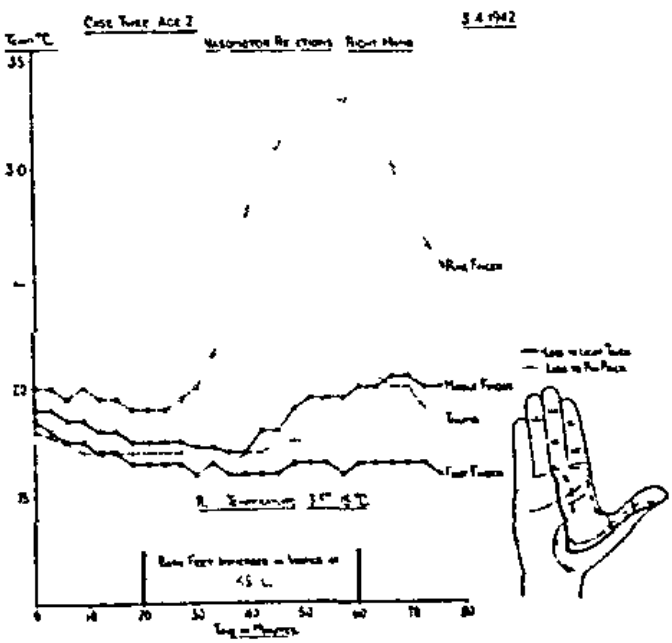

FIG 91

Case JT Right median nerve lesion, loss of sensation and vasomotor reactions four months after injury

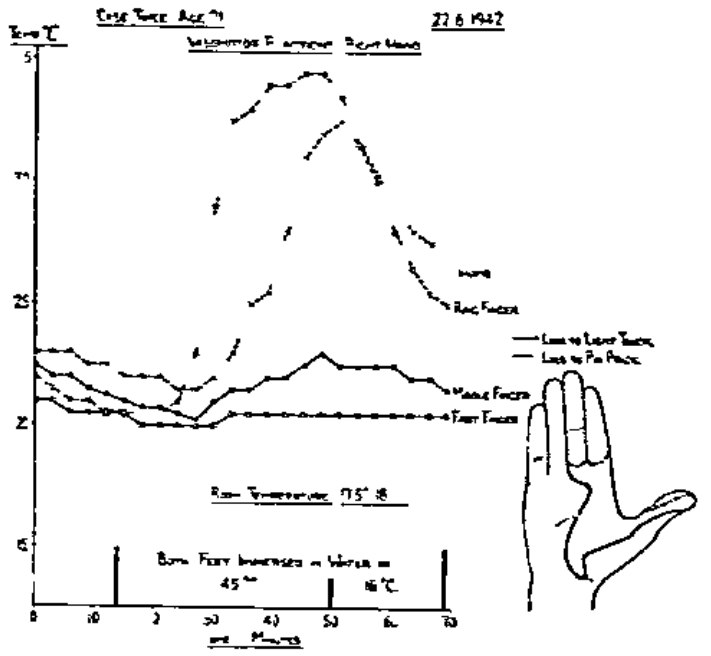

FIG 92
Case JT At seven months note recovery of vasomotor activity in thumb

limited Reference has already been made to the return of normal vasomotor activity in a case where nerve division was incomplete (p 114) Recovery of vasomotor function after complete nerve division will now be considered

Case JT Four months before coming under observation, a merchant navy officer injured the right median nerve in the palm with a revolver bullet Loss of sensation in the classical territory of the median nerve resulted A vasomotor test showed an absence of reflex vasomotor activity in the first three digits of the right hand (Fig 91) At operation the nerve was found to be intact, but the anterior surface was grooved where the bullet had passed The lesion was therefore an axonotmesis Seven months after the injury there was a good vasomotor response in the thumb, but not in the index or middle finger (Fig 92) By this time there had been recovery of pain sensation in the thumb At 11 months there was a good vasomotor response in all three affected digits (Fig 93) and pain sensation was present over the whole of the previously insensitive area Appreciation of cotton wool touches was still poor, and tactile discrimination grossly defective

In another case (JE) 2 years after a successful suture of the median nerve in the forearm reflex vasomotor activity in all digits of the affected hand was apparently normal (Fig 94) In this case also there was still an extensive area of anaesthesia but, except on the tips of the index and middle fingers, the response to painful stimuli was of the

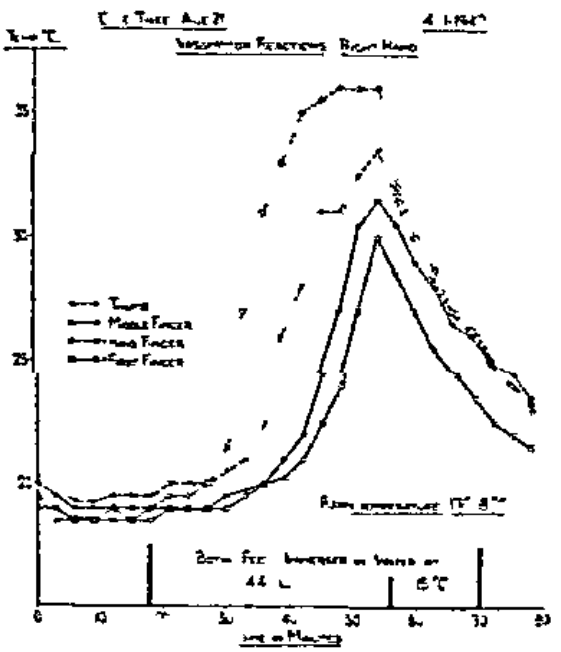

FIG 93
Case JT At eleven months vasomotor activity now almost normal

ill-localised, diffuse, unpleasant variety which always accompanies recovery after suture

After recovery of reflex vasodilatation, patients still complain of coldness of the affected digits, and after exposure to cold, digits which are partially re innervated become abnormally cold This agrees with the observation of Lewis (1936) who states that digits do not recover their normal warmth until *sensory* fibres have regenerated Further information upon this point is required, but it appears that the fibres responsible for axonal vasodilatation regenerate more slowly than do sympathetic vasoconstrictor fibres Since the latter appear to regenerate along with pain fibres, this suggests that the fibres responsible for axonal vasodilatation do not belong to the small unmyelinated fibre group This is further supported by Lewis's (1937) observation that during nerve asphyxia conduction in the fibres responsible for axonal vasodilatation is blocked early

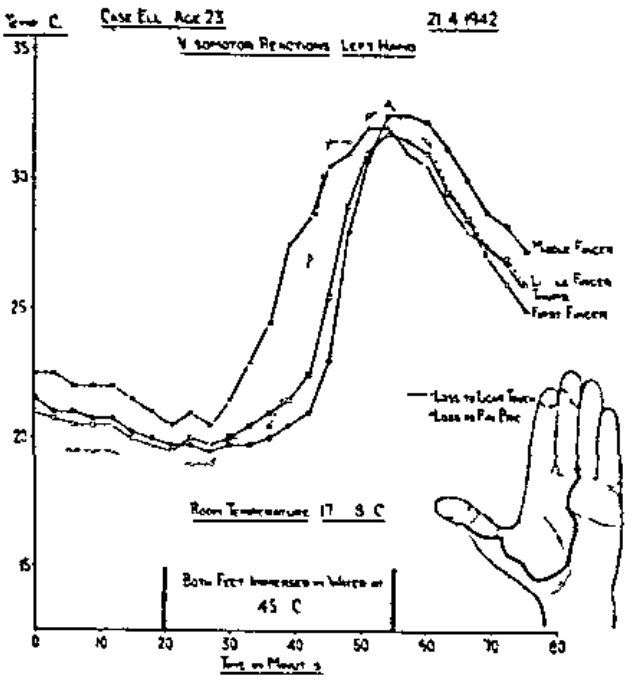

FIG 94

Case JE Left median nerve lesion to show recovery of sensation and vasomotor activity two years after a successful suture

Other factors may be concerned in the recovery of the normal warmth of denervated digits, for Lewis and Pickering (1936) observed that normal warmth did not return until 2 months after normal axonal vasodilatation had been observed

Nutritional changes also persist long after reflex vasomotor activity is normal Three years after interruption of the digital nerves to his left little finger, Sharpey Schafer (1930) observed that nail growth was still appreciably slower than normal At the time of the final vasomotor observations in the two cases reported above, there was still appreciable atrophy of the pulp of the index and middle fingers This is further evidence that such changes are non specific and do not depend upon the integrity of vasomotor fibres

SUMMARY

Observations upon the vasomotor disorders which accompany lesions of the peripheral nerves in man are presented There is no fundamental difference between the changes observed in the upper and lower limbs After division of a peripheral nerve, the vasomotor state of the denervated cutaneous area passes through two phases —

(1) An initial phase of vasodilatation due to the interruption of sympathetic vasoconstrictor fibres (the warm phase)

(2) A second and permanent phase in which the temperature of the area approximates to that of its environment (the cold phase)

No clear-cut distinction in time exists between these two phases The factors responsible for the change to the cold phase are not fully understood, but the most important are a lowering of local metabolism, sensitisation of denervated cutaneous blood vessels to circulating adrenalin, loss of afferent nerve fibres responsible for axonal vasodilatation, and the integrity of the innervation of the rest of the limb A digit which is incompletely denervated may show almost normal reflex vasomotor activity A completely denervated digit will not respond reflexly to changes in body temperature, but will respond to the local metabolic needs of the tissues Recovery of reflex vasomotor activity in a denervated digit does not result in a return of normal warmth this must await the regeneration of the fibres responsible for axonal vasodilatation The nutritional disturbances which occur in denervated digits are nonspecific and may be observed in other conditions Observations in both complete and incomplete nerve lesions indicate that, as regards their vulnerability, distribution and rate of recovery, vasomotor fibres resemble the small unmyelinated fibres subserving pain and sweating In incomplete lesions, dissociation between motor functions on the one hand and sensory and vasomotor functions on the other, is not uncommon dissociation between vasomotor and sensory functions is rare but may be observed Lesions which interfere with nerve conductivity without causing complete vasomotor paralysis result in a lowering of peripheral vasoconstrictor tone The present study has not revealed any evidence in favour of the hypothesis that there are vasodilator fibres within the peripheral nervous system of man

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CHAPTER EIGHT

THE IMMERSION FOOT SYNDROME

INTRODUCTION

THE term "immersion foot" has been coined during the recent war to describe a condition which occurs in extremities exposed to severe moist cold, characterised by chilling as opposed to freezing of the tissues, in this respect it differs from frostbite The term is neither accurate nor adequate, since the syndrome to which it is applied need not necessarily be produced by immersion, nor is it confined to the feet, but it is convenient, short and useful, and since it has been generally adopted both in this country and in America, there is no reason to discontinue its use The alternative "peripheral vasoneuropathy after chilling" (Ungley and Blackwood, 1942), although more comprehensive and accurate, lacks simplicity In this chapter "immersion foot" will be used to cover all cases of damage to peripheral tissues resulting from exposure to cold, short of freezing, including conditions described as "water-bite," "lifeboat leg," "sea boot foot," etc, because it is considered that the essential aetiological and pathological features of all these conditions are the same The descriptions of trench foot as it occurred in the last war (Cottet, 1919, Grattan, 1922, Thomson, 1939), in the recent Spanish Civil War (Rabut, 1939 Monsaigneon, 1940), and in the Allied armies during the winter of 1943-44 (Edwards *et al*, 1944, Boland *et al*, 1945), present a general clinical picture similar to that of immersion foot and the two conditions appear to be akin if not identical

From time immemorial, immersion foot must have occurred amongst seafarers and those exposed to cold and wet, but prior to 1940 there was an extraordinary dearth of medical literature upon the subject It is probable that this was largely because the condition was confused and identified with frostbite, a confusion persisting even at the present day (see Brownrigg, 1943) Critchley (1943) has collected presumptive evidence of the occurrence of immersion foot as long ago as 1727, he quotes several instances where swelling and mortification of the feet were recorded in the survivors of shipwrecks, and in explorers in arctic and antarctic waters It might be expected that cases would occur even in peace-time, for example in fishermen liable to spend long periods in all weathers almost knee deep in water and fish, yet medical officers who deal with merchant seamen and fishermen cannot recollect having seen such cases There are usually several boats in company at fishing grounds, so that in the event of any mishap the survivors are rapidly rescued, and when a fishing boat is wrecked near land, the men are either drowned or quickly rescued by coastguards

Records of " trench foot " go back to earliest times, and in the early months of the present war cases were seen which had been labelled " trench foot in a sailor " The first mention of the term " immersion foot " in print appears to have been by Greene (1941) Subsequently descriptions of the syndrome have been published in this country by Ungley and Blackwood (1942), Ungley (1943c), Critchley (1943) and Ungley *et al* (1945), and in America by Webster *et al* (1942), White (1943) and Patterson and Anderson (1945)

Although immersion foot is seen most frequently in ship wrecked sailors who have spent considerable periods in lifeboats, or clinging to rafts or Carley floats,[1] with their lower limbs immersed in cold sea water, it may occur in any conditions in which the extremities are exposed to cold and wet , for example in sailors who have spent several days under arctic conditions on deck or in their bunks, without removing their rubber sea-boots or socks (" sea boot foot ") , in Royal Air Force personnel who have had to bale out over the sea and spend several hours in the water or in rubber dinghies , in a guardsman who deserted from his unit in central Scotland and lay out in the hills for over a week , and in Royal Air Force personnel who have spent many hours on exposed Scottish hillsides after aeroplane crashes

CLINICAL FEATURES

This chapter is concerned primarily with the vasomotor disorders of the immersion foot syndrome, but a general consideration of the natural history and clinical features of the condition is necessary

(1) **During Exposure.**—The typical history given by survivors is that during exposure the immersed limbs are numb, powerless and feel as if they were no longer present They are seldom painful, although they may be very tender if knocked or rubbed Tingling and itching are rare complaints Occasionally cramps are felt in the legs Although in all probability it has begun earlier, it is not until several hours or even days have passed that swelling of the feet is noted Frequently the first evidence of swelling is that boots begin to feel tight, are removed, and cannot be replaced At first the colour of unprotected feet is often noted to be a vivid red, and at sea-water temperatures near sea freezing point this colour may be maintained, but at higher temperatures the feet tend to become " sickly white," mottled, bluish or even black in colour The tissues of the feet become friable and after minor injuries areas of blistering and even gangrene occur After rescue the affected limbs pass through three distinct phases these have been described as pre hyperaemic, hyperaemic and post-hyperaemic (Ungley and Blackwood, 1942)

(2) **Pre-hyperaemic Stage.**—This phase is a direct continuation of the events occurring during exposure , the feet continue to feel numb and are frequently described by survivors as being ' like lumps of lead " Pain is absent, but the feet may be tender to pressure If survivors attempt to walk, they usually find they are unable to maintain their balance and have to be assisted or carried If able to walk, they describe the sensation as " walking on air " or " walking on cotton

[1] See Critchley (1943) for a description of these rescue craft

wool" Movements of ankles and toes are absent or impaired, and there is sensory disturbance of "stocking" type which varies from hypaesthesia and hypalgesia in mild cases to complete loss of all modalities of sensation in severe cases In the case of an airman exposed on a hillside for 46 hours, it was stated that immediately after rescue he could not feel a pin prick until waist level was reached In the early stages it is common for sensory loss to extend as high as the tibial tuberosity

The feet are usually described as being white or only slightly discoloured, but the legs frequently show large black, blue, greenish or yellowish patches The amount of swelling and blistering depends upon the severity of the exposure, but swelling may extend as high as the knees and blisters may cover the whole of the dorsum of the foot and malleolar region During the pre-hyperaemic stage it is difficult to be certain of areas that are to become gangrenous

Except in the mildest cases, during this phase the dorsalis pedis and posterior tibial pulses are absent There is no actual record in which femoral and popliteal pulses were noted to be absent, although severe cases are frequently referred to as being "pulseless to the knee" The pulses as a rule remain absent and do not return until the onset of the hyperaemia As tested by the return of colour after blanching by finger pressure, the capillary circulation is certainly very sluggish, and it is likely that in many cases actual stasis may be present

(3) Hyperaemic Stage.—In most cases the development of the hyperaemic stage seems to occur with extraordinary rapidity If patients are left with the feet exposed to the air, and only the trunk and proximal portions of the limbs covered, the feet will become hyperaemic in from 2 to 48 hours, depending upon the severity of the original exposure The onset of hyperaemia may be accelerated by warming the feet, as happened in a number of cases in the early months of the war, but this procedure is mentioned only to be condemned

Pain is the most prominent symptom of the hyperaemic stage As a rule the feet remain painless in the pre hyperaemic stage but pain on movement of the feet may be noted before hyperaemia develops With the development of hyperaemia pain appears, varying from a very intense "pins and needles" feeling to a severe burning, throbbing pain which can be relieved only by injections of morphine The pain begins rapidly and increases in severity to reach its maximum in 24-36 hours It is usually referred to the dorsum of the foot and frequently to the margins of blistered areas or to areas of incipient gangrene The patients themselves are conscious of the relation of the pain to the heat, and if lying in bed with the feet covered, will thrust them beyond the bedclothes to obtain relief[1] Though pain may begin to abate after the first 48 hours and in mild cases may disappear within that period, it may persist and be very severe for much longer A second type of pain develops later, usually from about the 7th to 10th day after rescue This consists of a "shooting," "stabbing" or "jumping" pain which begins in the middle of the foot and radiates to the tips of the toes Shooting pains are also felt occasionally in

[1] Pain may also be relieved by cooling with a fan or ice-bags (see p 139)

insteps, dorsum and the malleoli These pains are spontaneous, but may be aggravated by movement, heat, sensory examinations, and later by walking or standing Webster *et al* (1942) have noted that their onset is preceded by an intensification of the burning pain over the foot, but in the present series this has not been observed

Although to the patient pain is the most prominent feature of this phase, to the observer the heat and redness of the affected extremities are the most striking features Portions of the limbs previously cold and waxy become hot to the touch, and of a pale reddish or livid colour The hyperaemia usually develops proximally and thereafter spreads rapidly down the limb, but this is not always the case When fully developed, the maximal area of hyperaemia does not correspond to the territory of distribution of any nerve or blood vessel, but frequently bears a striking relation to the level of immersion or to the most proximal level at which colour or temperature changes were noted immediately after rescue The hyperaemia will extend right up to and form a very distinct line of demarcation around areas of developing gangrene

Hyperaemia is associated with a return of pulsation in the main arteries of the foot The earliest recorded return of pulsation in the dorsalis pedis artery has been 2½ hours after rescue (Ungley and Blackwood, 1942) Pulsation may return at any time during the first 48 hours Failure of the pulse to return during this period indicates an unfavourable outcome When pulsation does return, it very rapidly becomes full and bounding, and it is usually possible to see pulsation in the dorsalis pedis artery In one case in the hyperaemic stage it was even possible to see pulsation in the collateral artery which runs in front of the lateral malleolus (perforating branch of the peroneal artery) Associated with this return of pulsation, there are other evidences of an exceedingly active circulation If the feet are allowed to be dependent, they congest with extraordinary rapidity, becoming a deep cyanotic colour in which both red and blue are blended , on elevation the feet blanch almost instantaneously After blanching by finger pressure the return of colour is now more rapid than on a control limb[1] It appears that during this phase there is widespread vascular dilatation, and that arteries, veins, capillaries and probably arteriovenous anastomoses are all widely open

In the early hyperaemic stage there is dryness not only of the feet but often as high as the knee Critchley (1943) mentions a hot, moist, red foot, but this appears to be somewhat unusual Within a few days the area of anhidrosis shrinks to correspond very accurately with the area of sensory loss to cotton wool touches

Associated with the hyperaemia there may be a marked increase in the amount of swelling of the limb, and areas not previously blistered may become so Common sites for the appearance of blisters are over the metatarso phalangeal joint of the great toe, over the malleoli and heels, and along the outer border of the foot During the early stages of the swelling, the tissues are very tense and do not pit readily on

[1] In some cases it has been found impossible to blanch discoloured areas by finger pressure , in these extravasated blood must be present in the tissues

pressure In 2 cases it has been possible, shortly after rescue, to obtain oedema fluid from the swollen feet The protein content of this fluid was estimated —

Case LEP		5 69 per cent total protein
Case DAL	Right foot	2 09 per cent total protein
	Left foot	2 58 per cent total protein
	Left foot	2 00 per cent albumin
	Left foot	0 58 per cent globulin

It is to be noted that the figures in the second case are very similar to that (3 per cent) quoted by Lewis (1942) for the protein content of fluid obtained from a hand after immersion for 2 hours in water at 5°C , and higher than that found in simple subcutaneous transudates Fluid obtained from the blisters is usually glairy or straw coloured in appearance, but may be blood stained The protein content of the blister fluid is similar to that of blood serum (8 94 gm /100 c c in Case LEP , 7 8 gm 100 c c in Case LIN)

As the hyperaemia develops, there is a rapid recovery of sensory functions Within 6-12 hours the area of sensory loss in cases previously insensitive as high as the tibial tuberosity may have receded to cover only the toes, sole and a tongue like area on the dorsum of the foot From an observation on one case it is possible that during the early hyperaemic stage there is a greater recovery of sensation than that to be observed some hours later, suggesting that the increased swelling during this phase may be a factor in determining the final sensory picture Associated with the return of sensation there is frequently a marked degree of hyperaesthesia and hyperalgesia, so that the affected parts may be acutely tender even to the lightest pressure, and may even be intolerant of the pressure of bedclothes or dressings in contact with them In the fully developed hyperaemic stage the distribution of the loss of sensation is usually of sock or carpet slipper " type, but it may be patchy, for example islets of anaesthesia over the malleoli are not uncommon Analgesia is frequently more extensive in its distribution than anaesthesia to cotton wool touches

Recovery of motor activity in the ankle foot and toes may be noted during the early hyperaemic phase but it is usually imperfect owing to the gross amount of swelling When swelling subsides, wasting of the intrinsic muscles of the affected extremity is noted hollowing of the sole and marked clawing of the toes occurs A strange feature of this wasting is its tendency to persist for long periods after there has been a considerable return of power and when sensation is almost normal The wasted muscles exhibit diminished electrical excitability

Areas of incipient gangrene may fail to warm up and remain blue cold and covered with blisters The presence of such an area need not necessarily indicate that the whole of the tissues of the limb at and distal to the area are in danger of becoming gangrenous Forty-eight hours after rescue the condition of a foot in which eventually only the toes or portions of the toes are to be lost, may appear most alarming Petechial haemorrhages and even large areas of ecchymosis frequently develop over areas which have been the site of mild, and in many cases, unnoticed traumata

It is in this stage of intense hyperaemia, and usually complaining of quite considerable pain, that most survivors reach hospital

The duration of the hyperaemic stage is variable, and depends upon the severity of the exposure It is probable that even in the mildest cases there is a transient period of hyperaemia which passes unnoticed In a typical case of immersion foot the duration of the phase is usually from 6 to 10 weeks Towards the end of this period the hyperaemia begins to show signs of instability, and the affected extremities may on occasion be found to be cool or cold As the hyperaemia passes off, pain abates , the constant burning pain has usually disappeared earlier, but the shooting, stabbing pains disappear about this time by a process of recession, that is, pains which at first shoot from the foot into the toes gradually recede until they are felt only in the tips of the toes

(4) **Post-hyperaemic Stage** —The transition from hyperaemic to post-hyperaemic stage is never abrupt After a short period of instability in which stimuli such as a walk in a cold atmosphere, standing with the feet on a cold floor, a tepid bath or fan cooling (Ungley, 1943a), may cause the hitherto warm extremities to become cool and remain so for several hours, the hands or feet become cold and remain permanently so For this phase Sir Thomas Lewis suggested the descriptive term 'algid state" It is to be noted that not every case exhibits a post-hyperaemic stage , mild cases may pass directly from the phase of warmth to normality

In this phase the extremities are cold-sensitive, that is, on exposure to cold they cool to an abnormal degree and thereafter do not warm in a normal manner The appearance of the feet in this stage may be comparatively normal, but they may also show abnormal pallor or an extreme degree of cyanosis In the post hyperaemic stage spontaneous excess sweating is commonly observed Patients complain that when walking, particularly on a warm day, their socks become soaked with perspiration, and even in a cool room the cool or cold feet may be noted to sweat excessively Sweat rashes may develop in areas where sweating is heaviest This *hyperhidrosis resembles that of causalgia and other irritative nerve lesions in that it* is most obvious in response to emotional or noxious stimuli, whereas over the affected area sweating in response to body-heating may be diminished In the post-hyperaemic stage these two symptoms, sensitivity to cold and excess sweating, are the common complaints, but patients may also complain of delayed swelling of the feet when walking is resumed, of a return of tingling and shooting pains, and of a recurrence of blisters

The symptoms of the post hyperaemic stage may persist for very long periods Critchley (1943) quotes Professor Orlov of Archangel as stating that the after effects of immersion foot may persist for a life-time and that relapses are common Certainly cases considered to have been relatively mildly affected may complain of symptoms 18 months to 2 years after rescue Apart from the symptoms described above, the late sequels include pain in the calf suggestive of intermittent claudication, failure of healing in ulcers formed under blisters and by the removal of gangrenous tissue, and changes in the bones and joints of the feet (post traumatic osteoporosis , hallux rigidus, etc) Many patients remain well so long as they are ashore but

may have a recurrence of symptoms when they return to sea in northern latitudes, for example —

Case BLA A merchant navy officer, aged 23, came under observation in April, 1944 Two years previously he had been adrift in an open boat in the North Atlantic for 17 days He had suffered from a moderately severe degree of immersion foot for which he received treatment in Nova Scotia There had not been any loss of tissue He returned to this country and spent one year ashore During this time his only complaints were slight excess sweating and occasional shooting pains in the feet and toes In April 1943, he was considered fit to return to sea He made two trips across the South Atlantic without any trouble His next voyage was across the North Atlantic in September When 3 days out and on watch, the left foot became very cold and painfully numb", he was unable to walk and had to be carried below When his boots were removed, the foot was seen to be a deep purple colour and it was thought it might become gangrenous He was in hospital in Canada for one month and appeared to recover, but on the return voyage the foot again gave similar trouble When admitted to hospital in this country, the feet appeared normal, the left felt slightly colder than the right and both showed some hyperhidrosis

(5) **Immersion Hand** —In most instances the hands are not immersed, and thus are exposed to an air temperature which, in latitudes where immersion foot occurs, is considerably lower than sea temperature Nevertheless the hands suffer less than the feet In only one patient in the present series have the hands been more severely affected than the feet

Case LIN This patient, aged 30 and a pawnbroker in civil life, had spent 4 years in a relatively sedentary job in the army He was transferred to a mountain unit, and in the early days of March, while on an exercise in the central highlands of Scotland, was overcome by weakness and collapsed A blizzard was blowing at the time, and there was snow on the ground He was lost for 36 hours During this period he was unable to walk, and crawled and stumbled about the hills He had three pairs of gloves on his hands but these soon became soaked and subsequently froze His feet were well protected with two pairs of socks and strong climbing boots The state of his hands 3 days and 5 weeks after rescue is shown in Figs 95 and 96 His feet were relatively unaffected

Minor degrees of involvement of the hands probably occur in all cases, but it is rare for the lesions in the hands to be severe Since the non immersed hands may be exposed to very low temperatures, it is possible for frostbite to occur in the hands coincidentally with immersion foot (Ungley *et al*, 1945)

During exposure the hands become numb, swollen and clumsy, and patients find that they have difficulty in performing movements such as undoing buckles or unscrewing the caps of flasks As in the case of the feet, the hands are less severely affected in those who are active (baling, rowing, etc) If one hand is more exposed than its fellow, it will suffer more severely, an interesting example may be cited —

Case DAL An R A F sergeant was exposed on a hillside for 46 hours The only nourishment he was able to obtain during this period was snow which he scraped

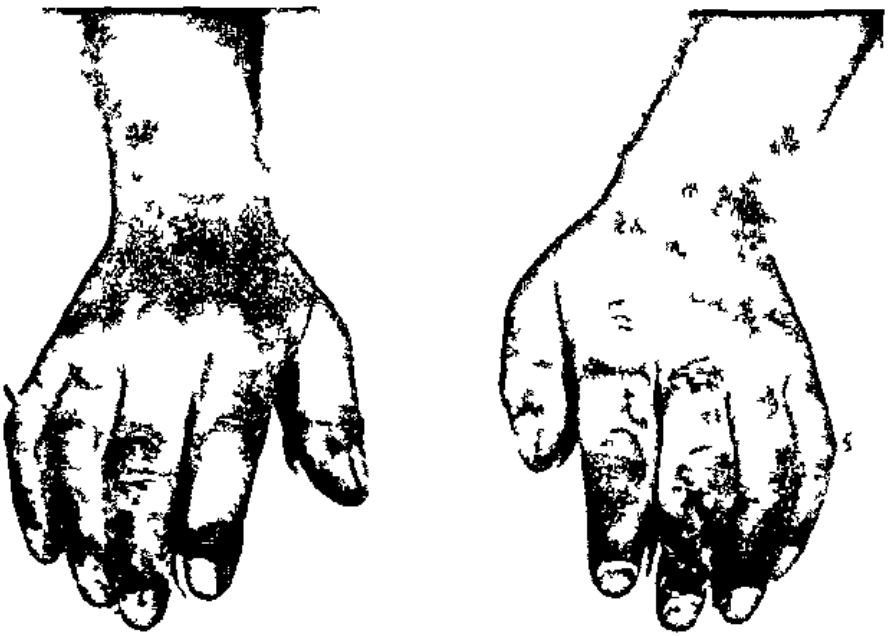

FIG 95
Case LIN Appearance of hands three days after rescue

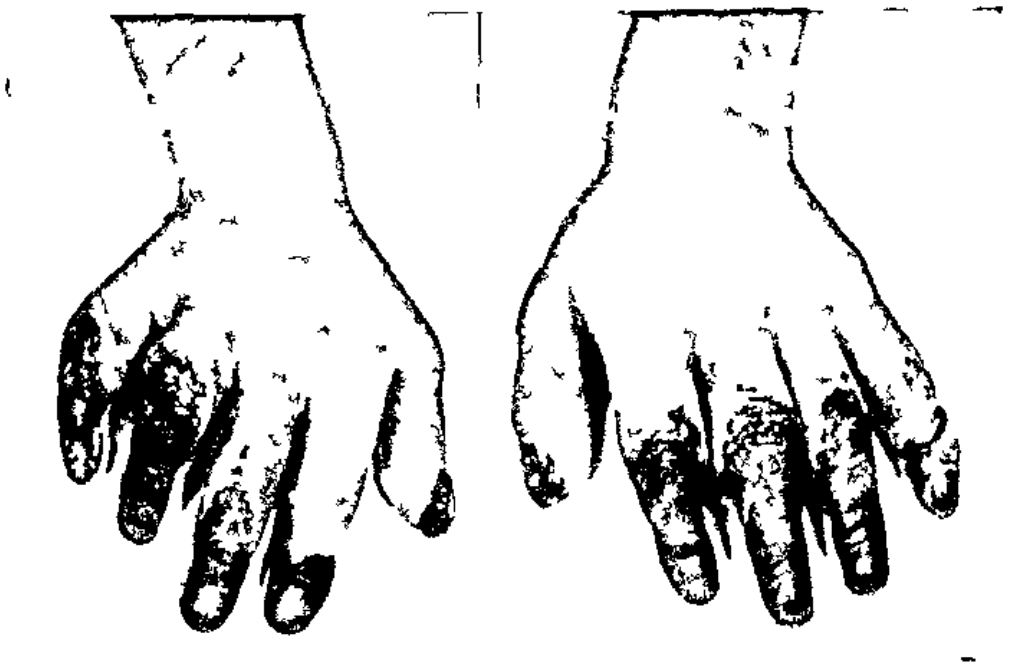

FIG 96
Case LIN Appearance of hands five weeks after rescue

up with his left hand Twelve hours after rescue there appeared to be little difference between the hands both were slightly swollen, warm and dry, and movements were normal Four weeks later there was wasting of the small muscles of both hands, but the left hand was more severely affected than the right, the muscles being exceedingly wasted, without voluntary power and not responding to the faradic current In contrast to this extreme motor disability, there was little, if any, sensory disturbance in either hand

Like the feet, the hands pass through a period of hyperaemia, and shortly after rescue become hot and throbbing, intense paraesthesiae are felt in the finger tips Swelling is usually present but is not as prominent as in the feet This phase does not last for more than a day or two, and as the swelling subsides wasting of the intrinsic muscles of the hand becomes apparent The wasting of the intrinsic muscles is more pronounced in the hands than in the feet, giving rise to an appearance very similar to that of progressive muscular atrophy The skin assumes a dirty yellow colour and peels off, leaving healthy pink skin Sensory disorders in the hand are rarely pronounced Pain is an uncommon symptom, but many patients complain of tingling in the digits on exposure to cold, or when the hands are becoming warm Objective sensory findings are usually confined to hypaesthesia and hypal gesia of the finger tips Even in those who have had little evidence of immersion hand when first examined, cold sensitivity is frequently observed This may take the form of vasospastic attacks similar to the Raynaud phenomenon

Patients whose hands have been affected almost invariably complain that during cold weather or when their hands are exposed to any form of cold, they become stiff, numb and much weaker than normally In the later stages of immersion hand, hyperhidrosis is also a prominent symptom, but it appears to subside more rapidly in the hand than the foot Critchley (1943) has described permanent deformities of the fingers due to contracture of the flexor tendons, and atrophy of the subcutaneous tissue, and has suggested an analogy between immersion hand and Volkmann s ischaemia He also suggests that the wasting of the small muscles of the hand is not due to the direct effect of cold and wet, but is due to a reflex constriction of the vasa nervorum causing what he describes as a " neuropathy a frigore "

SKIN TEMPERATURE OBSERVATIONS

It is not practical to make observations during the period of exposure From observations in certain short term experiments in which volunteers have immersed their limbs in water, it is known that the temperature of the extremity falls rapidly to within 1 2°C of the water temperature (Lewis, 1942) Lewis states that when the whole hand is immersed in cold water, the fluctuations in temperature which are seen when only a digit is immersed (Lewis, 1930), do not take place Holling (1943) found that 9 minutes after immersion in water at 3 3°C there was a slight secondary rise in the temperature of the foot

The earliest records of skin temperature in the present series have been made 9 hours after rescue in the case of the feet, and 12 hours after rescue in the case of

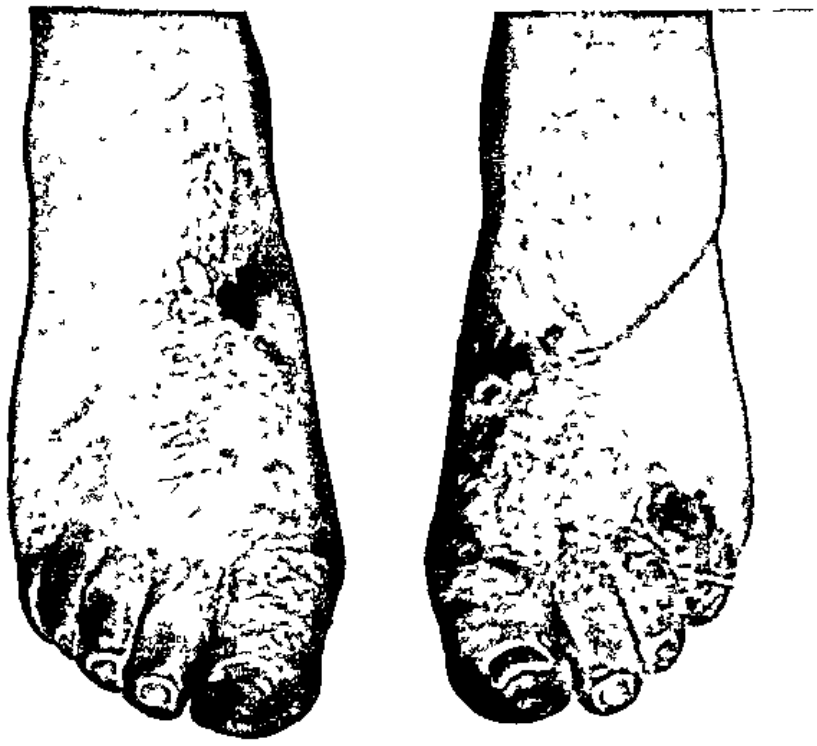

FIG. 97
Case LEP. Appearance of feet eight days after rescue.

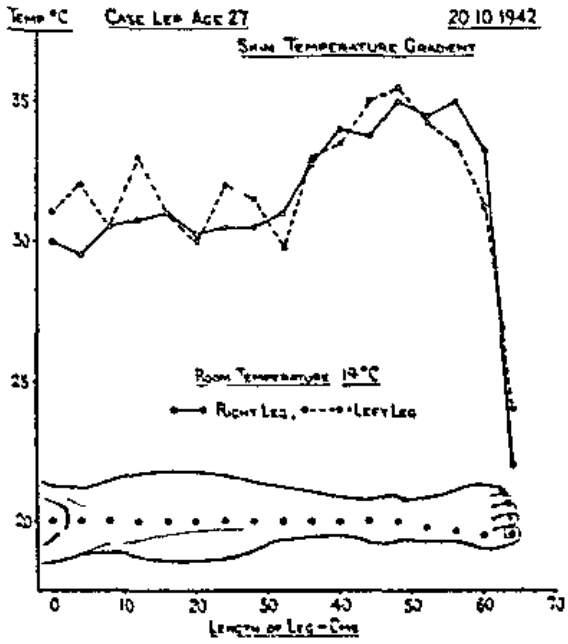

FIG. 98
Case LEP. Skin temperature gradients of lower limbs on day on which Fig 97 was taken.

the hands In Case DAL (p 128) the feet were already hot by the time the patient was seen, but the toes of the left foot felt cool Thermocouples attached to the great and little toes recorded temperatures of 29 5 and 30°C respectively, and within the next 3 hours the temperature rose to 34-35 C, this level being maintained for the next 24 hours In Case LIN (p 128) the temperatures of the nail beds of the middle fingers recorded in the period from 12 to 16 hours after rescue were right 31-32°C , left 27-30°C at a room temperature of 19 5-20°C Yet it is to be noted that subsequently portions of both these digits became gangrenous (Fig 96)

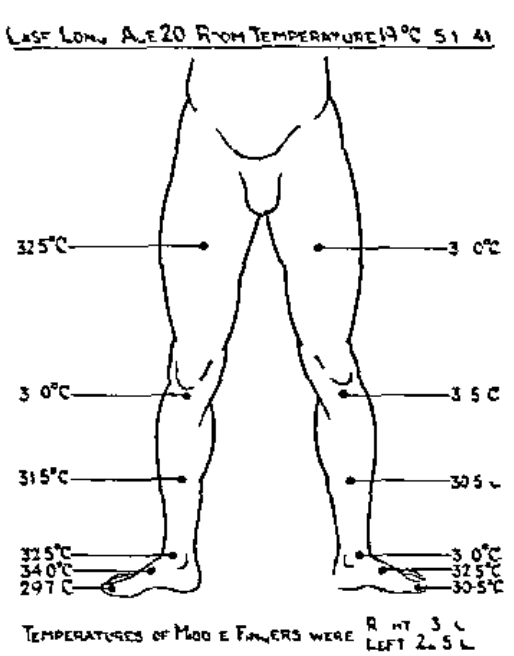

FIG 99
Case LON Four weeks after exposure skin temperature gradients note high resting temperature of feet compared with fingers

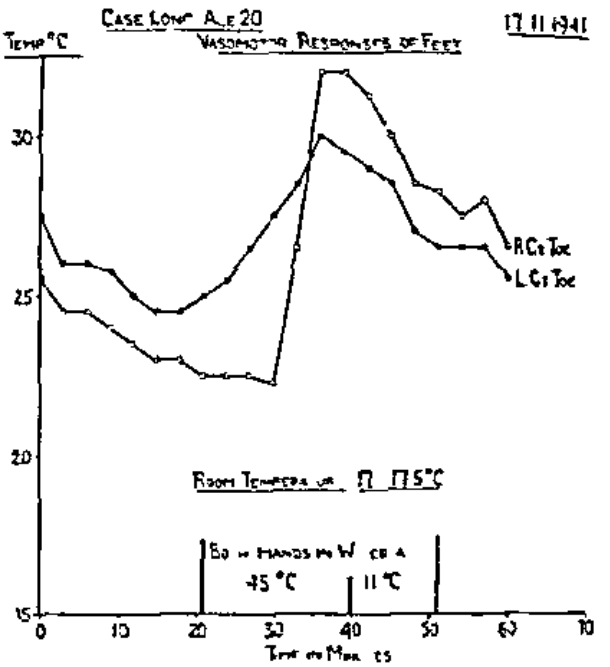

FIG 100
Case LON Four weeks after exposure vasomotor reactions note high initial temperature of toes and diminished response in left foot

Once the hyperaemic stage is fully developed, the whole extremity, except for gangrenous areas, is very much warmer than the more proximal portions of the limb (Figs 97 and 98), that is, the normal vasoconstrictor gradient is abolished In cases where there is no gangrene of the digits, the toes remain hot and there is no evidence of reflex vasomotor activity in response to immersion of the arms in hot or cold water (Ungley *et al* 1945) At a later stage slight cooling of the extremities becomes apparent on exposure in a cool room the extremities cool slightly, but there is still evidence of an abnormal lowering of vasoconstrictor tone in the feet so that the toes remain warmer than the fingers (Fig 99) At this stage reflex vasomotor activity may be demonstrated in the digits, but the response is frequently of a gradual type as compared with the normal abrupt rise and fall in temperature (Fig 100) It is at this stage that hyperaemia becomes unstable and on some days the extremities may be noted to be quite cool

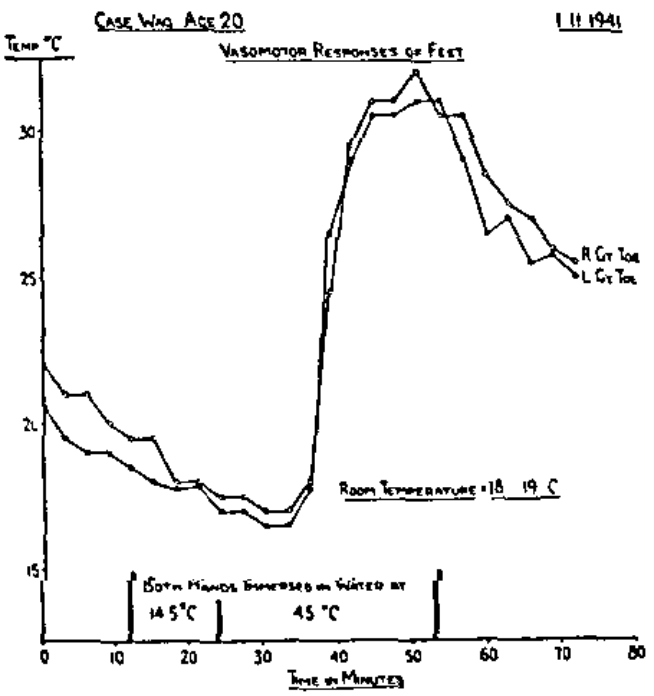

FIG 101

Case WAG Three weeks after exposure, normal vasomotor reactions

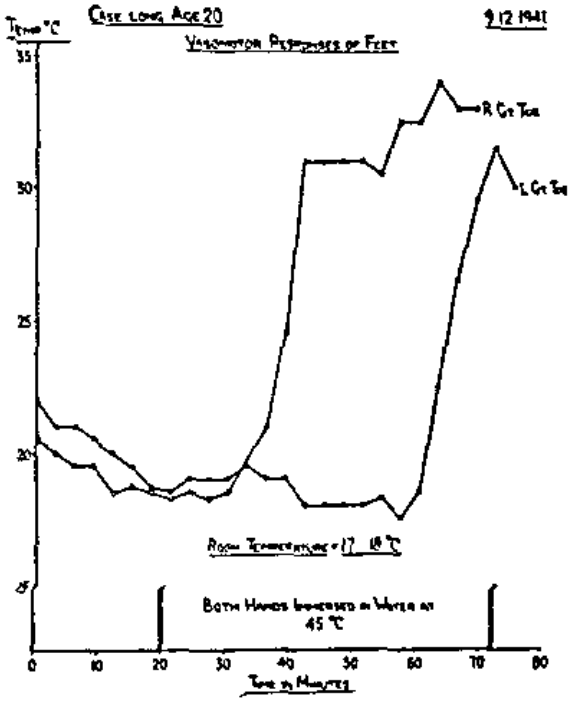

FIG 102

Case LON Seven weeks after exposure, vasomotor reactions, note delay before vasodilatation in left foot (cf Fig 100)

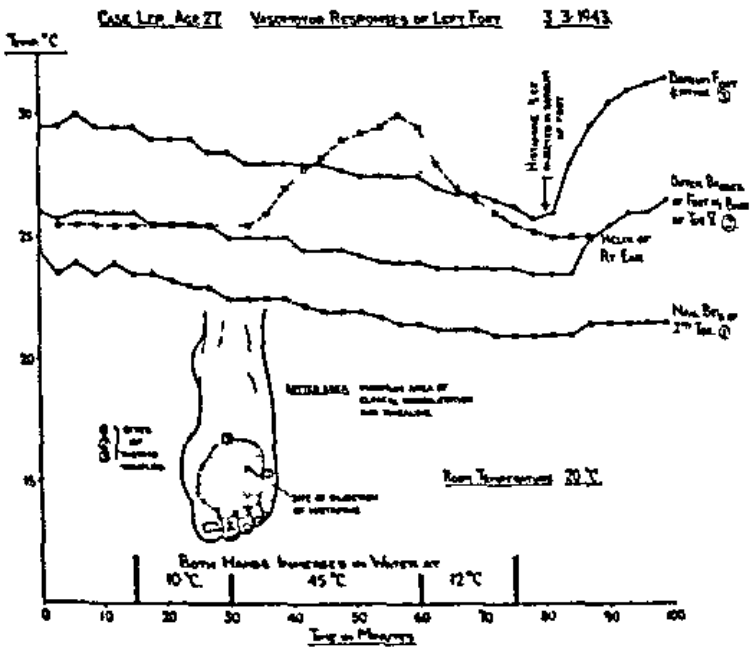

FIG 103

Case LEP Five months after exposure, vasomotor reactions; note failure of reflex vasodilatation in left foot but good response to the injection of histamine The diagram shows the sites of the thermocouples and the extent of the flare resulting from the injection of histamine

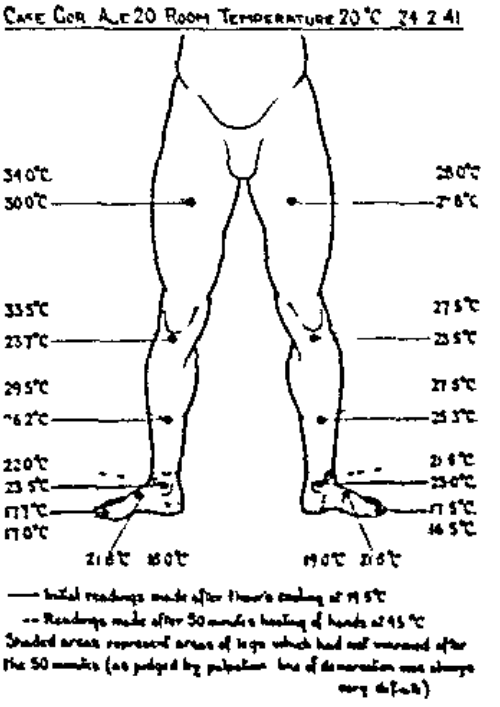

FIG. 104

Case GOR Five months after exposure; skin temperature gradients before and after body heating, note failure of vasodilatation in the feet

Once a normal vasoconstrictor gradient has been restored and the feet are permanently cool or cold (post hyperaemic stage), many abnormalities of reflex vasomotor activity may be observed Mild cases may show normal vasomotor reactions 3 weeks after rescue (Fig 101) Other cases may show a conspicuous delay before normal vasodilatation occurs (Fig 102, left foot) In more severe cases the feet remain cool and there is a complete absence of reflex vasomotor activity (Fig 103) It is to be noted that this occurs although the initial temperature of the feet is relatively high (24-26°C) and that it is apparently not due to any obstruction in the cutaneous blood vessels, because a local injection of histamine causes a conspicuous rise in temperature In one case which showed this failure of vasodilatation in the feet, there was a marked rise in temperature in the more proximal portions of the limbs (Fig 104) and a striking line of demarcation between the area which remained cold and that exhibiting vasodilatation

Cases complaining of symptoms months or years after exposure may have normal vasomotor reactions, for example Case BLA (p 128) showed a vasodilatation in the great toes of 14°C in 12 minutes, commencing 11 minutes after immersion of the hands in hot water It is in this group that Telford (1943) has advocated the performance of sympathectomy A left lumbar sympathectomy was performed in this case and the immediate result was excellent

DISCUSSION

(*a*) **The Effects of Cold**—Cold is the one essential factor in the causation of immersion foot The effect of cold upon the tissues was extensively studied by Lake (1917) and more recently by Sir Thomas Lewis (Lewis and Love, 1926 , Lewis, 1930 1941 and 1942) In isolated tissues the critical temperature at which irreversible changes occur is -6°C By virtue of the property of super-cooling, intact tissues may be cooled to a much lower level before actual freezing occurs Once the critical level is reached, certain irreversible physico-chemical changes in cell protoplasm occur and recovery is impossible This is what happens in true frostbite , there is a central zone of devitalised tissue surrounded by a zone in which tissue damage from cold is minimal Immersion foot, however, is due to chilling rather than freezing of the tissues There is a lack of general agreement as to the amount of damage which may result from the direct effects of exposure to temperatures within the range (2 10 C) which causes immersion foot Many writers (Greene, 1941, 1943 , Lake, 1942) believe that in both immersion foot and trench foot little or no damage is done during the period of exposure, and that harm is done chiefly during the period of thawing During the period of exposure profound disturbances in the metabolism of the chilled tissues must occur It is known that, as the scale of temperature is descended, anabolism ceases before katabolism It is not certain at which temperature level these metabolic changes occur, but from his work with tissue cultures Lake (1942) believes that in the zone between 25 C and 10 C products of tissue katabolism are accumulating At temperatures lower than this metabolism ceases entirely and tissues are in a state of suspended animation where they require neither

oxygen nor nutriment and so cannot become ischaemic These observations have given rise to the hypothesis that damage to chilled limbs occurs not during the phase of exposure but while the temperature of the limb is passing through the critical phase of imbalanced metabolism between 10 and 25°C This zone will be crossed twice, during the period of chilling and during warming, and in the latter process may be crossed very rapidly Metabolites accumulated during this phase are responsible for the violent vasodilatation which takes place This in turn leads to exudation which is responsible for the neurological and nutritional lesions which follow (Lake, 1917 and 1942) It is doubtful if this hypothesis, which is based on observations on isolated tissues, is directly applicable to the events which occur when a human limb is chilled Experimental evidence that damage to tissues may occur actually during the period of exposure has been provided by Smith, Ritchie and Dawson (1915-16), and more recently by Blackwood and Russell (1943 and 1945) It is therefore important in discussing the pathogenesis of the immersion foot syndrome that full consideration should be given to the events which are known or may be presumed to occur during the period of exposure

Exposure of an extremity to cold causes peripheral vasoconstriction This is brought about partly by the local effect of cold upon blood vessels and partly by nervous reflexes through sympathetic pathways If, to the local effect of cold upon the extremity, there is added the effect of general body cooling which must be present in most cases of immersion foot, the vasoconstriction may be very profound The experiments of Talbott (1941) on general hypothermia have shown that although severe vasoconstriction may be present so that for several hours peripheral pulses may be impalpable and the blood pressure unrecordable, yet thrombosis does not occur and blood continues to flow in the arteries This is presumably what occurs in immersion foot, since during exposure and in the pre-hyperaemic stage the extremity is cold, pale or mottled, the veins are collapsed and the pulses impalpable, and then within a matter of hours it becomes hot, flushed and there is every indication of an exceedingly active circulation The clinical evidence is therefore in favour of the hypothesis that during exposure and the pre hyperaemic stage intense vasoconstriction is the predominant vascular feature of immersion foot In an attack of the Raynaud phenomenon, vasoconstriction is sufficient to cause complete arrest of the circulation in a digit It is therefore justifiable to assume that in immersion foot the vasoconstriction is of itself capable of cutting off the blood supply to the chilled extremity Unless, as Lake found in his tissue cultures, a state of suspended animation of the tissues is present during this phase, ischaemia must occur and in any interpretation of later developments it is impossible to dissociate the direct effects of cold and the secondary effects of ischaemia upon the tissues

When the extremities are exposed to low temperature, vasoconstriction may not be the only factor contributing to ischaemia of the peripheral tissues Opinion on the important question of arterial thrombosis is not unanimous In experiments in which rats' tails were exposed to environmental conditions similar to those which cause immersion foot in man, Blackwood and Russell (1943) did not find any evidence of organic vascular obstruction In experimental true frostbite similar

findings have been reported by Greene (1943) and others Friedman (1945) who has recently reviewed the literature on this subject quotes several workers who have reported arterial thrombosis as a sequel to exposure to cold and mentions that there is considerable disagreement as to whether thrombosis follows tissue freezing only or may occur as a result of protracted chilling In the majority of cases it is exceedingly difficult to decide whether thrombosis has occured during the period of exposure or as a result of the events which take place during subsequent warming Considering the problem from the clinical aspect it is difficult to believe that arterial thrombosis is a primary pathological change in cases of immersion foot, in certain cases thrombosis may occur as a secondary process in response to additional trauma

Thus far the effect of cold upon larger vessels of the calibre of arteries and arterioles has been considered, the reaction of the minute vessels is also important A relatively short exposure to cold is sufficient to cause dilatation of the minute cutaneous vessels, the red reaction which follows the immersion of an extremity in cold water is caused by dilatation of minute vessels which are filled with oxygenated blood (Lewis, 1927) The effect of severe or protracted cold upon the minute vessels is more complex Rotnes and Kreyberg (1931 and 1932) studied the effects of experimental freezing of rabbits' ears by a new method of intra vital staining with lithium carmine (a diffusible stain) and Indian ink (a non-diffusible stain) They found that areas frozen by carbon dioxide snow and then allowed to thaw showed a local hyperaemia with transudation of fluid into the tissue spaces If the Indian ink was injected 15 minutes after freezing all the vessels in the hyperaemic area were visualised Injection of the Indian ink 24 hours later gave an entirely different picture except in the case of an area frozen for only one second, the larger blood vessels could be seen running across the hyperaemic area but the minute vessels were no longer visualised Microscopical study of the specimens showed that the minute vessels were dilated and tightly packed with red blood cells They interpreted these findings as indicating that during the period of low temperature the walls of the minute vessels were damaged so that when the circulation returned plasma leaked through them leaving the red cells stranded in the lumen—the phenomenon of stasis Further experimental work upon true frostbite by Greene (1943) and Lange and Boyd (1945) has confirmed these findings Kreyberg (1945) has also applied his theory of intravascular stasis to the tissue damage which follows protracted exposure to low temperature insufficient to freeze the tissues From what has been said above it is apparent that during exposure the peripheral tissues are subject to the dual effect of chilling and ischaemia The walls of the minute vessels are particularly susceptible to anoxia and will therefore suffer early damage, clinically this is confirmed by the appearance of oedema as the first sign of prolonged chilling of an extremity (Lewis, 1942) At this stage the reduction in metabolism brought about by the low temperature, and vasoconstriction in the larger arteries, prevent the process from developing further, but when the circulation to the part is restored, transudation will increase, stasis will occur, and, if damage to the vessel walls has been sufficiently severe, extravasation of red cells may also take place The importance of this theory is two-fold first, except in cases where the exposure has been very severe, the chilled

tissues are not dead at the time of rescue but may later become necrotic from cutting off of their blood supply by intravascular stasis, secondly, it is thought (Bigelow, 1942) that stasis, unlike thrombosis, is not necessarily an irreversible process, in some cases stasis may progress and become an irreversible process, the red blood cells conglutinated[1] in the vessels become necrotic and form intravascular hyaline masses which permanently block the lumina of the vessels, in other cases a condition of pre-stasis may be present, that is the condition of the circulation in the minute vessels is such that any additional trauma (for example, injudicious warming, rubbing or further chilling) may tip the balance and cause stasis to occur

(*b*) **The Cause of the Hyperaemia**—The transition to the hyperaemic stage may be presumed to occur when the warmth of the body and the proximal portions of the limbs is sufficient to overcome the vasoconstriction induced by the exposure to cold If this hypothesis is correct, it is not surprising that the development of the hyperaemia is rapid In normal limbs in response to a rise in body temperature the release of peripheral vasoconstriction causes a very rapid rise in skin temperature The excessive vasodilatation which is present in the hyperaemic stage may be due to three factors inflammation and the release of vasodilator metabolites, local damage to vessels and vasoconstrictor paralysis It is to be noted that skin temperature which in the present study has been used as an index of the hyperaemia, probably does not give an accurate estimate of the condition in the early stages The temperature of the skin cannot rise above a level which represents a resultant between blood temperature and environmental temperature This maximum is in the neighbourhood of 35°C Digits will frequently be as warm as this without any appearance of intense hyperaemia In the hyperaemic stage of immersion foot, accurate measurements of blood flow to the extremities would probably show a considerable increase over those obtained from a recently sympathectomised extremity where vasoconstrictor paralysis is the only factor causing the hyperaemia

Sir Thomas Lewis (1941) demonstrated that an aseptic type of inflammation occurs in tissues exposed to low temperature The vasodilatation which succeeds a brief period of exposure to cold has been shown by Lewis (1930) to be the result of an axon reflex causing the release of a relatively stable vasodilator substance (*H-substance*) A similar vasodilator substance is responsible for the reactive hyperaemia which follows a period of circulatory arrest (p 54) During the period of chilling and ischaemia vasodilator metabolites will accumulate in the tissues and when the circulation through the larger vessels is restored will cause an initial intense hyperaemia Once an active circulation is established, these, however stable, will be rapidly washed away from the tissues, and, unless a continued release of such substances is postulated they cannot be the cause of a vasodilatation the duration of which is measured in weeks rather than days Bacterial infection probably plays little part in the early stages of the hyperaemic phase but may be a factor later when blisters, ulcers and gangrene are present

[1] Kreyberg prefers this term to "agglutinate" since the latter has acquired a specific meaning in pathology

The effect of low temperature upon the blood vessels has already been considered Clinically, the deep red or blue colour of the feet and the remarkable changes in colour that take place when the feet are elevated or dependent, the presence of swelling and areas of ecchymosis all indicate that during the acute hyperaemic stage there is dilatation and damage to the walls of the minute cutaneous vessels The pathological state of these vessels has been described by Friedman (1945) "The capillaries and small vessels in the papillary loops, the sub papillary plexus and networks about the sweat glands and appendages and the subcutaneous plexus in and about the fat lobules were as clearly outlined as in tissue injected for teaching purposes" These changes are probably not permanent, in specimens obtained 8 weeks to 26 months after exposure Blackwood (1944) did not find any significant changes in the capillaries

In both experimental and human biopsy material severe damage to peripheral nerves is observed (Blackwood and Russell, 1943 and 1945, Blackwood, 1944, Large and Heinbecker, 1944, Friedman, 1945) In the main nerves of the foot the majority of the fibres are degenerated and those, if any, which escape are of large calibre Sympathetic vasoconstrictor fibres are of small calibre and are known to be relatively susceptible to cold (Bickford, 1939), so that it is very unlikely that they will escape The blood vessels of the foot will therefore be subjected to a post-ganglionic sympathectomy A week after exposure skin temperature gradients from affected limbs are very similar to those from sympathectomised limbs The standard sympathectomy performed for the lower limb is predominantly preganglionic, and it is unwise to compare further the hyperaemia of immersion foot with that in a sympathectomised limb Complete division of the sciatic nerve results in the interruption of all postganglionic sympathetic fibres to the foot (except for a few in the saphenous nerve) Such lesions produce a complete vasomotor paralysis in the toes, resulting in an initially warm, pale foot and later in a foot the surface temperature of which varies with that of the environment The duration of the initial hyperaemia is probably of the order of 21 days, and there is not the wide fluctuation in the duration of the hyperaemia that is seen in cases of immersion foot Sensitisation of the cutaneous blood vessels to circulating adrenalin is one of the characteristics of a post-ganglionic sympathectomy (White and Smithwick, 1942) and Ungley *et al* (1945) have shown that this phenomenon is present in the later hyperaemic phase of immersion foot Collateral clinical evidence of nerve damage in the form of loss of sensation, muscle wasting and anhidrosis is present It is, therefore, justifiable to assume that a vasoconstrictor paralysis is an important factor in the hyperaemic stage of immersion foot

(c) **The Value of Cold Therapy** —The value of cold as a form of therapy in the treatment of the so-called "cryopathies'[1] has recently aroused considerable discussion In the early hyperaemic stage of immersion foot there is no doubt that cooling either by ice bags (Webster *et al*, 1942), a fan (Ungley, 1943a), or specially

[1] The author is not in favour of the general adoption of this term The first component does not as in the case of the other pathies refer to the affected tissue but to the causative agent (Greek κρυος cold)

designed cooling cabinets such as those described by Greene (1942) and Bigelow and Lanyon (1944), gives considerable symptomatic relief from pain and hyperaesthesia, and its use on these grounds alone is probably justifiable Once hyperaemia has developed, cooling by these methods may reduce the surface temperature of the extremity to 23-26°C At this temperature patients are comfortable but further cooling tends to cause discomfort (Ungley, 1943a) Safford and Nathanson (1944) state that the optimum cutaneous temperature for protracted therapeutic cooling is 70°F (21°C), this is best obtained by a blast of cold air and may be maintained for several days if need be

Although there is evidence of a very rapid and active circulation to the extremity, the presence of a warm cyanosed skin when the limb is allowed to be dependent is an indication that there is relative anoxia of the superficial tissues (Lewis, 1927) The increase in surface temperature is an important factor in causing this anoxia because it increases the rapidity of metabolic processes and thus raises the tissue demands for oxygen Surface cooling by any of the methods described reduces cell metabolism and thereby tends to bring tissue demands within reach of the available blood supply White (1943) believes that anoxia of nerve endings is responsible for the early pain in immersion foot, and that the relief afforded by cooling is a direct result of a more balanced metabolism This argument appears to be sound, and the use of cold therapy under these circumstances is rational provided that the temperature of the tissues is not allowed to fall below 10°C at temperatures lower than this the dissociation of oxyhaemoglobin almost ceases (Brown and Hill, 1923)

There is less general agreement regarding the virtue of maintaining chilling of the extremity immediately after rescue The direct application of heat to any extremity which is in danger of ischaemia is unreservedly condemned Lewis (1936) states "It is quite certain that the warming or heating will increase the metabolism of the tissues and thus increase the blood flow requirement" This applies even more strongly to an extremity which is severely chilled The argument in favour of maintaining chilling is that the rate of warming may be controlled and the dangers of subsequent tissue damage due to exudation from damaged vessels lessened Lewis (1942) has shown that cold below 15°C exerts upon the tissues an injurious effect which increases as the scale of temperature is descended Safford and Nathanson (1944) state that tissue temperatures lower than 10 C maintained for more than twelve hours are dangerous if there is any circulatory obstruction, slight pressure or subsequent rapid warming It therefore appears to the author to be wrong to maintain any chilled extremity at a temperature below 15°C for longer than is absolutely necessary Elevation[1] and exposure of the affected extremities in a cool atmosphere (18-20 C) appears to be a logical, and, from personal experience, a satisfactory method of first-aid and definitive treatment Measures directed to increase the blood flow to the affected extremities such as reflex vasodilatation and sympathectomies either temporary (novocaine or alcohol block), or permanent (operation), are also to be condemned, the increase in blood flow caused by these

[1] Patients as a rule will tolerate only moderate elevation (30-45°) of the feet

procedures is likely to lead to increased intravascular pressure, greater exudation and probable greater damage to tissues

(*d*) **The Late Vascular Phenomena.**—After a few days the intense hyperaemia subsides, the extremities may then return to normal or show signs of a continued but milder hyperaemia lasting for 6-8 weeks In mild cases, where a return of vascular tone and reflex vasomotor activity is rapid, any interruption of vasoconstrictor fibres must be temporary, and in these cases the release of vasodilator metabolites in response to the prolonged chilling and ischaemia is the main factor in causing hyperaemia After the initial intense hyperaemia, moderately severe cases show a partial recovery of vasoconstrictor tone and a diminished response to immersion of the arms in hot and cold water The vasomotor disturbances in this group are similar to those described by Wilkins and Kolb (1941) in cases of polyneuritis, *and to those found by the author in cases of incomplete division of the sciatic nerve* (p 113) Goldstone and Corbett (1944) believe that a peripheral neuritis is the *predominant clinical feature of immersion foot This is undoubtedly true of the* moderately severe case, but the neuritis differs from all other forms in the patchy nature of the destruction of peripheral neurons

The persistent coldness of the extremities, the sensitisation to cold and the failure of reflex vasodilatation which are seen in the late stages of severe cases are more difficult to explain A denervated area of skin in a limb with an otherwise intact innervation is similarly susceptible to the influence of cold (Richards, 1943) Cutaneous denervation is undoubtedly one factor in causing the persistent coldness of the extremities in the late stages of immersion foot, but it does not account for all cases since in many the coldness is present when observations upon sensation and sweating indicate that nerve regeneration is complete

Exposure to severe cold, whether dry cold or wet cold, sensitises the peripheral blood vessels so that thereafter they are more susceptible to the effects of milder degrees of cold The mechanism is obscure, but is presumably similar to that responsible for the Raynaud phenomenon In the latter, the digital arteries are sensitised either as the result of repeated exposure to mild degrees of cold or because of some inherent " local fault " in the arteries themselves [1]

Intense vasoconstriction of sympathetic origin may account for persistent coldness of the extremities and failure of reflex vasodilatation The presence of excess sweating is suggestive of increased sympathetic activity Reflex vasodilatation, however, fails to occur even when the initial temperature of the feet is fairly high (Fig 103 Gaylor, 1943) In 2 cases vasodilatation has failed to occur after spinal anaesthesia

Failure of reflex vasodilatation or a gradual rise in temperature may be the result of occlusion of the main arteries In the present series this was excluded on clinical grounds because the peripheral pulses were of good volume In one case (LEP, Figs 97, 98, 103) patency of the arteries of the foot was demonstrated by arteriography It is therefore apparent that the late vascular phenomena of immersion foot are present in cases with patent main arteries The possibility that smaller

[1] *This problem is discussed elsewhere (p 85)*

vessels of the calibre of arterioles are occluded requires further consideration In biopsies from cases of immersion foot 4 months after exposure, White and Warren (1944) found extensive fibrosis of subcutaneous tissue and superficial muscle They state "*The arterioles and venules show partial to almost complete occlusion* as a result of a great increase of the fibrous tissue in their walls The arteries and veins of larger calibre show the same type of fibrous thickening of the wall, but with a lesser degree of occlusion of the lumen" Similar findings have been reported by Friedman (1945) in a study of the pathology of trench foot Reflex vasodilatation is dependent chiefly upon the opening of arterioles and arteriovenous anastomoses A local interference with these structures in the skin and subcutaneous tissue such as White and Warren and Friedman describe *is precisely what would be expected from* a finding such as that shown in Fig 104 where a very definite localised area in each foot failed to show vasodilatation The observation recorded in Fig 103, however, is against such an hypothesis, in this case, after the failure of reflex vasodilatation the local injection of histamine caused a marked rise in temperature According to Lewis (1927) the response to histamine is the result of an arteriolar dilatation White and Warren (1944) suggest that in the late stages of immersion foot pain is due to constriction of nerve endings by interstitial tissue and collagen Vasoconstrictor nerves may also be affected in this cicatricial process and normal vasomotor responses disturbed

An alternative explanation has been put forward by Ungley (1943b) The late vascular phenomena are observed at a time when observations on sensation and sweating suggest that a certain amount of regeneration of damaged nerve fibres has taken place Ungley somewhat tentatively suggests that these phenomena are the *result of partial denervation or partial re-innervation of cutaneous blood vessels*, and the sensitisation of the blood vessels to chemical substances (adrenalin, sympathin) circulating in the blood stream or produced locally He believes that this, together with a local sensitivity to cold on the part of the blood vessels themselves, might well account for all the late vascular phenomena

SUMMARY

The origin and use of the term "immersion foot" are considered Personal observations upon a series of cases are presented *The clinical manifestations are* considered, and three phases, pre-hyperaemic, hyperaemic and post-hyperaemic described Attention is directed chiefly to the vascular disturbances of the syndrome During exposure and in the pre hyperaemic stage the feet are cold and pulseless Evidence points to intense vasoconstriction as the pathological basis of this stage, organic vascular occlusion probably does not occur Damage to minute vessels, probably the result of anoxia, causes an increased permeability of their walls When the circulation is restored, plasma leaks through the damaged walls leaving the corpuscles stranded in the lumen, thus causing an intravascular stasis In the hyperaemic stage there is an initial intense vasodilatation, succeeded, in all but the mildest cases, by a lesser degree of hyperaemia lasting for 6 to 8 weeks The initial intense

vasodilatation is the result of a local release of vasodilator metabolites in tissues injured by the cold damage to cutaneous vessels may also be a factor The later vasodilatation is the result of a vasoconstrictor paralysis and is due to damage to vasomotor fibres in the peripheral nerves The vascular disturbances of the post hyperaemic phase are an abnormal coldness of the feet and an undue sensitivity to cold on the part of the blood vessels which may manifest itself by attacks of the Raynaud phenomenon These disturbances are difficult to explain Denervation of cutaneous vessels partial or complete resulting in sensitisation of the vessels to the local constrictor action of cold or to circulating vasoconstrictor hormones and occlusion of arterioles by the deposition of fibrous tissue in the subcutaneous layer, are considered to be two possible explanations The value of cold therapy in cases of immersion foot is considered As a form of treatment immediately after rescue, its value is as yet unproven in the hyperaemic stage it has a definite value for the relief of pain

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CONCLUSION

" It is in the very nature of things that the study of disease, to be effective, must begin as it must end with disease itself, and that all knowledge applicable to human disease must owe its inspiration directly or indirectly, to intimate contact with *disease as this exists in living man* " (*Lewis, 1934*) *With this as precept, the peripheral* circulation in the limbs of man in both health and disease has been studied and an attempt has been made to explain the findings on the basis of well established conceptions of anatomy and physiology

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